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The Effect of Access to Prenatal Genetic Testing on Test Utilization and Birth Outcomes: Evidence from Down syndrome

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Abstract

Recent scientific advancements have greatly improved prenatal genetic testing technologies, which can now detect a wide array of genetic disorders at a high degree of accuracy. Down syndrome provides a unique context through which to analyze the effect of women's access to prenatal genetic tests on test utilization and birth outcomes. In particular, typically only women of Advanced Maternal Age (AMA)—that is, women aged 35 and older—have qualified for an amniocentesis, the most common prenatal diagnostic test for Down syndrome. Using Vital Statistics live birth data from 1989 to 2002, I exploit the arbitrary nature of this AMA amniocentesis eligibility cutoff by implementing a Regression Discontinuity (RD) design to quantify the effect of access to amniocentesis on amniocentesis use and birth outcomes. As a secondary component of my analysis, I explore whether the effect of access to amniocentesis shifted over the course of the 1990s, as alternative prenatal genetic tests for Down syndrome became available. I find that becoming eligible for an amniocentesis increased the probability a woman underwent an amniocentesis by 6.2 percentage points (or 62% relative to the mean take-up rate of women around the cutoff), but that the increase in amniocentesis take-up at age 35 diminished significantly throughout the late 1990s. This negative time-trend in amniocentesis take-up at age 35 implies that over the latter half of my sample period, many amniocentesis-eligible women substituted away from amniocentesis and towards alternative prenatal genetic tests for Down syndrome that presented less risk to the fetus. Finally, I find no evidence that women terminated pregnancies that tested positive for Down syndrome or that test access affected other birth outcomes.

Introduction

Genetic disorders are surprisingly common, affecting an estimated 12 million Americans (PR Newswire, 2010). Recent scientific advancements—such as the "unlocking" of the human genome—have dramatically improved researchers' understanding of genetic disorders. Importantly, one result of this scientific progress is improved prenatal genetic tests, which can detect genetic disorders at a high degree of accuracy and at a low risk to the fetus. Parents who undergo these prenatal genetic tests and learn that the fetus is affected by a genetic disorder may choose to terminate the pregnancy, or they may simply use this critical piece of information to better prepare for the type of care that their child will need after birth. The availability of these improved genetic testing technologies, then, has significant implications for families, and at a broader level, for the healthcare system as a whole. The use of these genetic tests—as well as any actions parents may take in response to the information provided to them by these tests—impacts families' healthcare expenditures, in terms of the types of healthcare services that families utilize and the magnitude of families' spending on healthcare services.

Overwhelmingly the most common chromosomal abnormality, Down syndrome is of particular interest. With a long and rich medical history that dates back to 1866, Down syndrome provides a powerful lens through which to explore the effects that the combination of (1) prenatal genetic testing technologies, and (2) recommendations for the use of these technologies, has had on women's choices and behavior. In order to capture the causal effect of access to prenatal genetic tests for Down syndrome on women's test utilization and their babies' corresponding birth outcomes, I exploit the fact that expectant mothers have historically been offered differential access to prenatal diagnostic tests for Down syndrome, based on their age. In

particular, typically only women of Advanced Maternal Age (AMA)—that is, women aged 35 and older—have qualified for an amniocentesis, the most common diagnostic test for Down syndrome. Critically, this AMA amniocentesis eligibility cutoff is (arguably) arbitrary, in the sense that there is not a "jump" in the probability that a woman has a child with Down syndrome at age 35. Utilizing the arbitrary construction of this cutoff, I implement a Regression Discontinuity (RD) design. Since the AMA amniocentesis eligibility threshold is arbitrary, women who are just of AMA should not be fundamentally different than women who are just too young to be labeled as AMA, which means that I can interpret any difference in amniocentesis take-up and Down syndrome incidence around the AMA threshold as the causal effect of amniocentesis eligibility.

Using Vital Statistics birth data from 1989 to 2002, I investigate three specific questions. First, I explore whether there is an increase in amniocentesis take-up once women reach AMA. Second, I examine whether this increase—if it exists—diminishes over time. This second component of my empirical analysis is motivated by the fact that, over the course of the 1990s, new prenatal screening tests for Down syndrome were introduced. These screening tests, which typically only require a small sample of the mother's blood, present substantially less risk to the fetus than an amniocentesis, and as a result, these new screening tests potentially made AMA women's differential access to amniocentesis less important. To test this hypothesis, I investigate whether amniocentesis take-up at age 35 declines over the course of 1989 to 2002, as these new screening tests became more widely available to pregnant women. Lastly, I exploit the AMA amniocentesis eligibility cutoff to examine the effect of amniocentesis access on birth outcomes. In particular, I explore whether there is a shift in either Down syndrome incidence or broader

measures of infant health (i.e., the baby's birth weight and five-minute Apgar score) at the AMA threshold.

The rest of this paper is organized as follows. Section 1 provides background information, and Section 2 reviews the relevant medical and economic literature. Section 3 describes the data, and Section 4 provides a graphical description of the data. Section 5 details my empirical strategy, Section 6 presents the main results, and Section 7 describes robustness checks and falsification tests. Finally, Section 8 concludes.

Section 1: Background

A Brief History of Down syndrome

A familiar genetic condition, Down syndrome affects roughly one in every 700 babies born in the U.S. each year (Parker, et al., 2010). Individuals who have Down syndrome are easily recognizable and share distinct physical traits, including a flattened facial profile, poor muscle tone, and upward-slanting eyes. In addition to these obvious physical markers, individuals who have Down syndrome typically experience developmental delays, and they often require special education services (Bull, 2011, and Schieve, et al., 2009). Furthermore, children with Down syndrome face an increased risk of developing acute lymphoblastic leukemia (ALL) and myeloid leukemia (Stewart, 2009), and roughly half of all babies born with Down syndrome have a congenital heart defect (Bull, 2011).

Even though Down syndrome undoubtedly predates the nineteenth century, Dr. John Langdon Down provided the first official documentation of Down syndrome in 1866. In his

highly influential—but wildly offensive—"Observations on an Ethnic Classification of Idiots," Down incorrectly attributes Down syndrome to "tuberculosis in the parents." Furthermore, in a thinly-disguised and ethnically-motivated insult, Down argues that individuals who have Down syndrome must be of Mongolian descent. (Dr. Down considered Mongolians to be an inferior people) (Down, 1866).[1] Constrained by nineteenth-century technological limits, Down's essay essentially remained the only component of the Down syndrome medical literature until 1933, when it was observed that the probability that a woman has a child with Down syndrome increases with maternal age (Penrose, 1933). These surface-level observations formed the bulk of scientists' understanding of Down syndrome until 1959, when Dr. Jérôme Lejeune discovered that Down syndrome is caused by a third copy of chromosome 21.

Dr. Lejeune's seminal breakthrough paved the way for a deeper understanding of Down syndrome. In particular, researchers quickly discovered that there are actually three types of Down syndrome: (1) Trisomy 21, (2) Translocation, and (3) Mosaicism. Consisting of 95% of all Down syndrome cases, Trisomy 21 is the most common form of Down syndrome, and in this type of Down syndrome, the extra copy of chromosome 21 attaches itself to the other two copies of chromosome 21. Translocation and mosaicism are substantially less prevalent than Trisomy 21, and they make up approximately 3% and 2% of all Down syndrome cases, respectively (Shin, et al., 2011). In the case of mosaicism, only some cells have a third copy of chromosome 21, meaning that individuals with mosaicism tend to display fewer characteristics associated with Down syndrome (Modi, et al., 2003). Interestingly, translocation is the only form of Down syndrome that is "inherited," in the sense that it is caused by extra genetic material in either the

[1] It was this hypothesis that led to individuals with Down syndrome being referred to as "Mongoloids" until the latter half of the twentieth century.

father or mother. With translocation, the extra copy of chromosome 21 attaches itself to a different pair of chromosomes (Fisher, 2013).

Prenatal Diagnostic and Screening Tests for Down syndrome

Sparked by Dr. Lejeune's 1959 discovery, the past half-century has been marked by seemingly continuous discoveries and improvements of prenatal genetic tests for Down syndrome. Prenatal genetic tests for Down syndrome have been available since 1966, when Mark Steele and William Breg first discovered that an amniocentesis—which involves removing a sample of fluid from the amniotic sac—allowed for chromosomal karyotyping and in-utero diagnoses of Down syndrome (Steele and Breg, 1966). Considering the fact that an amniocentesis involves injecting a rather large needle through the wall of the uterus, it is perhaps unsurprising that an amniocentesis carries a relatively high risk of miscarriage, at around 0.6% (Mayo Clinic, 2015). Amniocentesis and Chorionic Villus Sampling (CVS)—a less common diagnostic test for Down syndrome—were the only available types of prenatal genetic tests for Down syndrome until the mid-1980s.

Prenatal screening tests for Down syndrome were developed in the mid-1980s. In contrast to prenatal diagnostic tests for Down syndrome (like amniocentesis), prenatal screening tests for Down syndrome cannot definitively determine whether the fetus has Down syndrome. Rather, prenatal screening tests simply estimate the likelihood that the fetus has Down syndrome. Despite their lower degree of accuracy, screening tests offer one critical advantage over diagnostic tests: Unlike invasive diagnostic tests, screening tests for Down syndrome present effectively no risk to the fetus.

The first of these screening tests—simultaneously reported in 1984 by two different teams of researchers—measured a pregnant woman's second-trimester alpha-fetoprotein (αFP) levels (Merkatz, et al., 1984, and Cuckle, et al., 1984).[2] In 1988, the triple screen—which, in addition to measuring second-trimester maternal αFP levels, also measured second-trimester maternal unconjugated estriol (uE3) and human chorionic gonadotropin (HCG) levels[3]—was introduced (Wald, et al., 1988). Providing a more accurate risk assessment of the fetus' likelihood of having Down syndrome than the αFP test (Wald, et al., 1988), the triple test forms the foundation of current Down syndrome screening tests (Reynolds, 2010).

Two other notable prenatal screening tests for Down syndrome were discovered in the 1990s. In 1992, Kypros Nicolaides, et al. first suggested that ultrasounds that measure the thickness of the fluid on the back on the fetus' neck (fetal nuchal translucency, or FNT) could be used as a preliminary first-trimester screening test for Down syndrome (Nicolaides, et al., 1992). As the American College of Obstetricians and Gynecologists (ACOG) acknowledges, however, the first FNT tests faced several obstacles, namely that there was initially considerable variability in the test's ability to detect Down syndrome (ACOG, 2007). The last breakthrough in prenatal screening for Down syndrome in the 1990s was the quadruple screen. Adding inhibin-A to the triple screen, Wald, et al., demonstrated that the quadruple screen had higher detection rates—and importantly, lower false positive rates—than the triple screen (Wald, et al., 1996). Since 1996, several new prenatal screening tests for Down syndrome have been introduced—including the integrated and stepwise sequential screens—but these new screening tests are essentially only

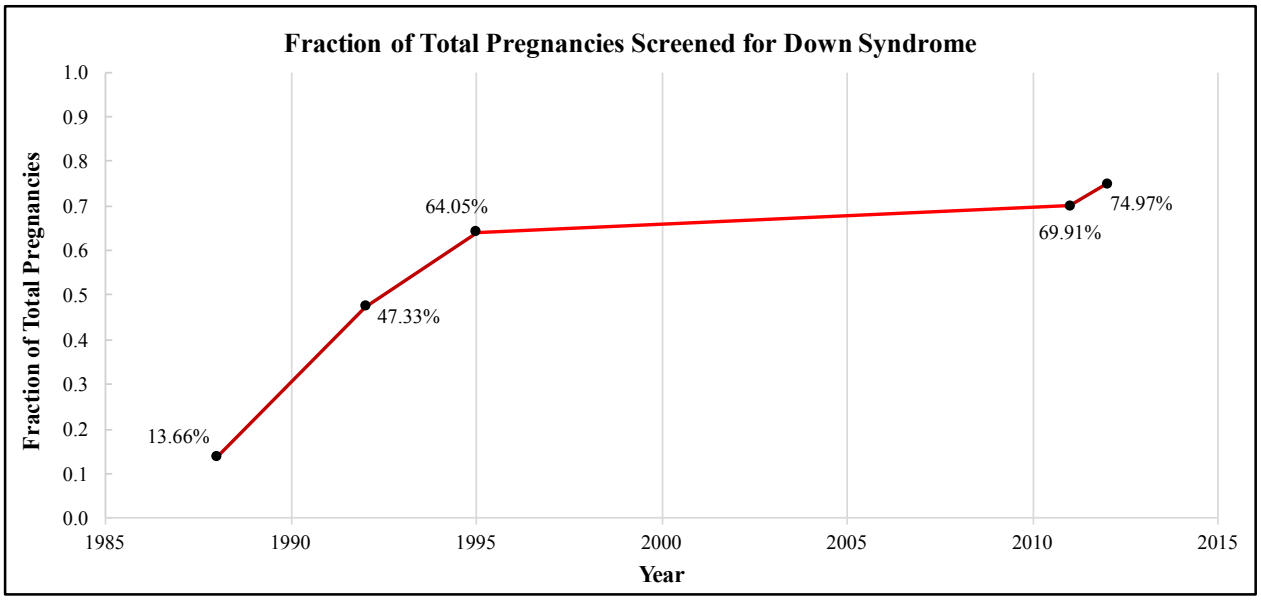
[2] Both sets of researchers found a strong negative association between the level of αFP in the mother's bloodstream during the second trimester and the probability that the fetus has Down syndrome.

[3] Wald, et al., found that maternal uE3 levels are depressed and that maternal HCG levels are elevated when the fetus has Down syndrome.

modifications to and expansions of the triple screen, quadruple screen, and FNT tests (ACOG, 2007).

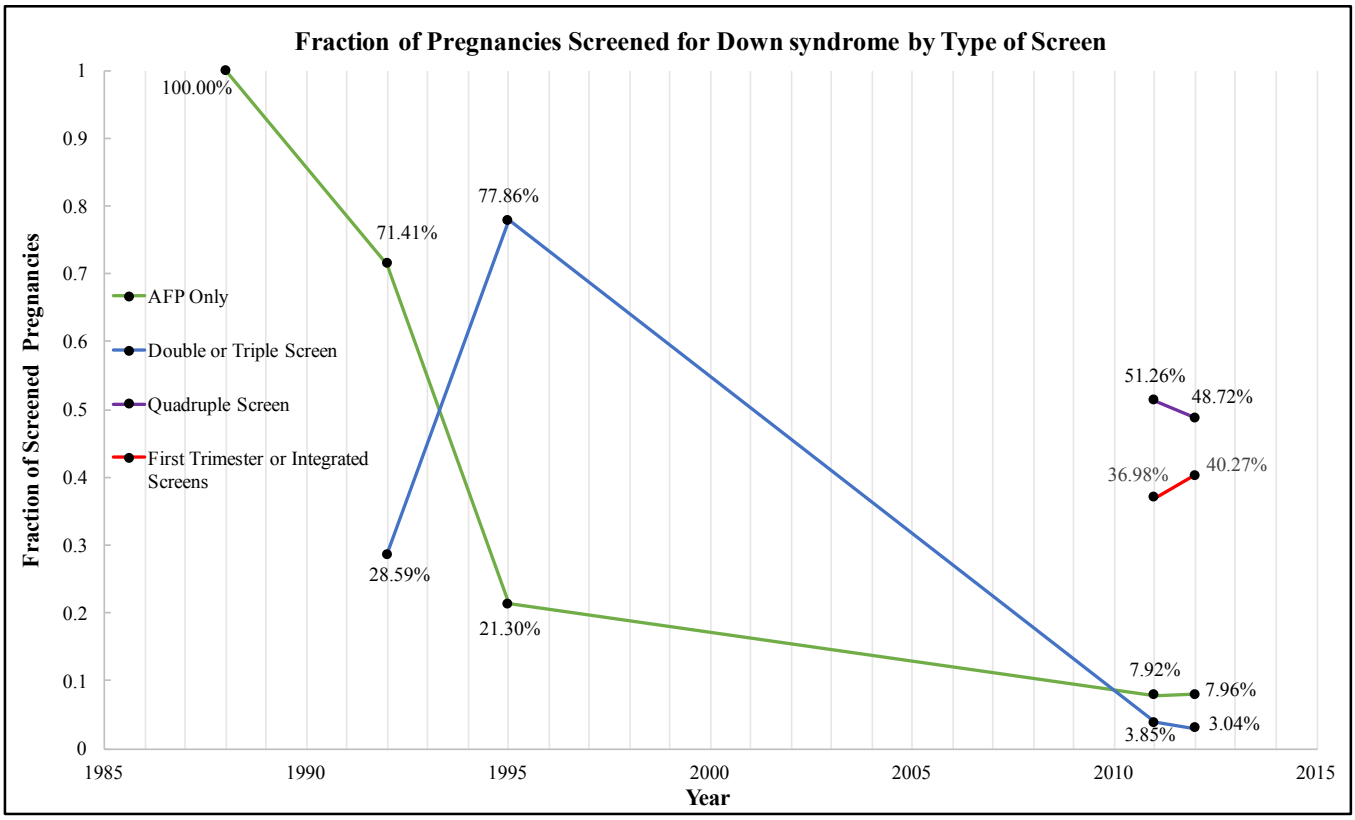
In order to fully understand the potential impact that these new screening tests had on amniocentesis use, it is also imperative to understand whether pregnant women actually had access to these screening tests. Although data on screening take-up is limited, Glenn Palomaki, et al., analyzed laboratory data to determine (1) the total fraction of pregnancies screened for Down syndrome (excluding amniocentesis), and (2) the fraction of screened pregnancies that underwent each type of screening test, in 1988, 1992, 1995, 2011, and 2012. This data, compiled from five separate reports, is graphically depicted in Figures 1 and 2.

Figure 1



Sources: Glenn Palomaki, et al. 1990; Palomaki, et al. 1993; Palomaki, et al. 1997; and Palomaki, et al. 2013

Figure 2



Sources: Glenn Palomaki, et al. 1990; Palomaki, et al. 1993; Palomaki, et al. 1997; and Palomaki, et al. 2013

Interestingly, Figure 1 shows that by as early as 1995, over 60% of pregnancies in the U.S. were being screened for Down syndrome. Considering that AMA women comprise between 10% and 20% of total births in any given year, the fact that a solid majority of pregnancies were being screened for Down syndrome by the mid-1990s implies that many non-AMA women were undergoing these screening tests. Moreover, Figure 2 shows that by 1995, the triple test had become the dominant screening test for Down syndrome. Unfortunately, data on quadruple screen take-up is not available until 2011, but in 2011—15 years after the test was introduced—the quadruple screen made up over 50% of that year's screenings. Overall, these two figures paint a fascinating picture, and together they suggest that prenatal genetic screening tests for Down syndrome were becoming increasingly more accessible and popular throughout the 1990s.

Even though the available data clearly suggests that pregnant women were taking advantage of these screening tests for Down syndrome, the causal impact of these screening tests on amniocentesis use is theoretically ambiguous. On the one hand, it is possible that these less-costly screening tests for Down syndrome served as "substitutes" for amniocentesis, particularly for AMA women. While Down syndrome screening tests are less accurate than an amniocentesis, AMA women may have replaced an amniocentesis with a screening test in order to minimize the risk presented to the fetus. In this case, one would expect the introduction of screening tests to decrease amniocentesis use among AMA women.

On the other hand, perhaps amniocentesis and Down syndrome screening tests can be considered to be "complementary goods." That is, it is possible that the widespread use of screening tests actually increased amniocentesis use among AMA women. Considering the fact that older mothers face a higher probability of giving birth to a child with Down syndrome, I would anticipate a greater fraction of AMA women's screening results to indicate that the fetus likely has Down syndrome, relative to non-AMA women. If a "positive" screening test induced a new "type" of AMA woman to undergo an amniocentesis—namely, women who were concerned about an amniocentesis' risks and would not have undergone an amniocentesis in the absence of a positive screening test result—this would potentially translate into a higher overall amniocentesis take-up rate for AMA women.[4] In the "Main Results" sections of this paper, I will actually use the Vital Statistics birth data to empirically estimate the extent to which

[4] While screening tests for Down syndrome provide an odds-ratio that estimates the likelihood that the fetus has Down syndrome, the results of these screening tests are then typically broken down into two categories: a "positive" result and a "negative" result. Women are typically told that the results of their screening test are positive if the odds of having a child with Down syndrome are determined to be greater than or equal to 1/270. Conversely, women are typically given a negative result if the odds of having a child with Down syndrome are calculated to be less than 1/270.

women's prenatal genetic testing decisions shifted in response to the introduction of new screening tests for Down syndrome.

Relevant Medical Guidelines for Prenatal Diagnostic Tests for Down syndrome

The previous section of this paper emphasizes recent technological improvements in prenatal genetic tests for Down syndrome. While the available data on utilization of screening tests for Down syndrome suggests that screening tests were available to a large subset—if not the entire universe—of pregnant women, medical guidelines have limited women's access to amniocentesis.

The National Institute of Health (NIH) issued the first of these guidelines in 1978. Citing amniocentesis' relatively high risk of miscarriage, the NIH stated that only AMA women should be able to undergo an amniocentesis[5] (Wertz and Fletcher, 1978). Following the NIH's lead, in 1983, the ACOG and the American Academy of Pediatrics (AAP) published their first *Guidelines for Perinatal Care*. In this document, the ACOG and AAP reinforced 35 as the maternal "cutoff age" for amniocentesis eligibility (ACOG and AAP, 1983). These guidelines were informed by an influential paper written by Ernest Hook, et al., which calculates 35 as the age at which the probability of having a child with Down syndrome equals the risk of a miscarriage from an amniocentesis (Hook, et al., 1983). From an expected utility standpoint, this reasoning seems to suggest that 35 is the maternal age at which the expected utility "loss" from an amniocentesis-caused miscarriage equals the expected utility "gain" from avoiding having a

[5] The NIH did establish several exceptions to this rule. For example, the NIH guidelines' stated that non-AMA women who had already given birth to a child with a chromosomal abnormality (such as Down syndrome) were also eligible for an amniocentesis.

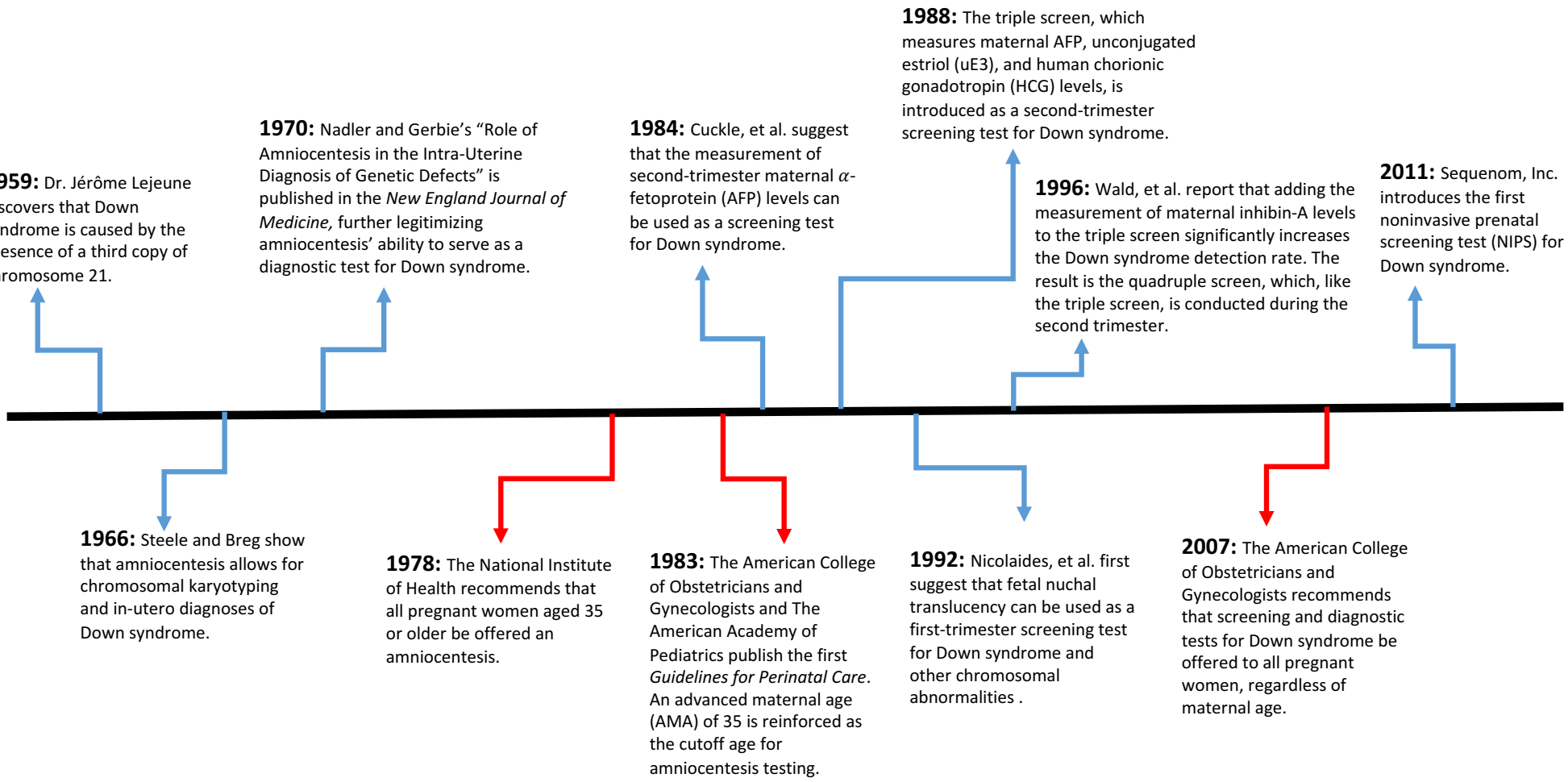
child with Down syndrome. Realistically, however, it is highly unlikely that expectant mothers place equal weight on these two potential outcomes.

These two guidelines formed the backbone of physicians' prenatal diagnostic testing recommendations until 2007. In 2007, the ACOG revised its 1983 recommendation, stating that, "All women—regardless of age—should have the option of invasive [diagnostic] testing" (ACOG, 2007).[6] A comprehensive timeline of these medical guidelines, juxtaposed with technological advances in Down syndrome prenatal genetic testing technology, is given in Figure 3.

[6] The ACOG justified its decision to open up amniocentesis access to all women with the following paragraph: "A woman's decision to have an amniocentesis or CVS is based on many factors, including the risk that the fetus will have a chromosomal abnormality, the risk of pregnancy loss from an invasive procedure, and the consequences of having an affected child if diagnostic testing is not done. Studies that have evaluated women's preferences have shown that women weigh these potential outcomes differently. The decision to offer invasive testing should take into account these preferences and should not be solely age based" (ACOG, 2007). This statement seems to suggest that the ACOG recognized that, even though at age 35, the probability of having a child with Down syndrome equals the probability having an amniocentesis-caused miscarriage, the utility "gain" from avoiding a child with Down syndrome at age 35 likely does not equal the utility "loss" from a miscarriage at age 35. Unfortunately, the ACOG does not reference the specific studies that influenced its decision.

Figure 3

A Timeline of Prenatal Genetic Testing for Down Syndrome



Section 2: Previous Literature

Perhaps unsurprisingly, the majority of the research that explores the effects of access to prenatal genetic tests for Down syndrome on women's choices can be found in the medical literature. In their paper "The Impact of a New National Screening Policy for Down syndrome in Denmark," Charlotte Ekelund, et al., report that a 2004 change in the Danish National Board of Health's prenatal genetic testing guidelines—which required physicians to offer screening tests for Down syndrome to all pregnant women—reduced the number of invasive diagnostic procedures by just over 50%. Even more interestingly, the authors find that the incidence of Down syndrome births fell by roughly 40% after the introduction of the policy (Ekelund, et al., 2008), which suggests that Danish women who underwent a screening test and received a positive result terminated the pregnancy.

Sian Morgan, et al. examines the impact of a similar prenatal genetic testing policy change in the United Kingdom (UK). In 2003, the UK's National Health Service (NHS) revised its "Model of Best Practice" to include a national screening policy for Down syndrome. In particular, this policy change opened up access to a first-trimester combined screening test for Down syndrome to all pregnant women.[7] Analyzing data submitted by all of England's cytogenetic laboratories from 2003 to 2011, Morgan, et al. report that 72% fewer invasive diagnostic tests were performed in 2011, relative to 2003 (Morgan, et al., 2013). Unfortunately, Morgan, et al. did not explore the impact of this new screening policy on Down syndrome incidence.

[7] A first-trimester combined screening test for Down syndrome includes an ultrasound that measures FNT, as well as a blood test that measures the levels of Pregnancy Associated Plasma Protein (PAPP-A) and free or total β-HCG in the mother's blood.

Seeking to dissect the broad macro-level observations reported in the medical literature, the economics literature that investigates the effects of women's access to prenatal genetic tests for Down syndrome primarily exploits older women's differential access to amniocentesis. In France, for example, only pregnant women who are aged 38 or older (or women whose preliminary screening tests estimated that the probability the fetus has Down syndrome is greater than 0.04%) are eligible to be reimbursed for an amniocentesis through France's national healthcare system. Capitalizing on this arbitrary reimbursement cutoff to implement a RD design, Christelle Garrouste, et al., find that qualifying for reimbursement increases the probability that a woman undergoes an amniocentesis by 55 percentage points. In other words, the authors find that pregnant women's prenatal genetic testing decisions respond strongly to monetary incentives (Garrouste, et al., 2015).

Eduardo Fajnzylber, et al. develop a dynamic model that uses expected utility theory to predict a woman's "optimal" amniocentesis choice, based on her age and number of other children. Fajnzylber, et al. argue that the cost of an amniocentesis actually rises with maternal age, because in the case of an amniocentesis-caused miscarriage, it is harder for older women to "replace" a miscarriage with another pregnancy.

The authors' model generates two important predictions. First, a simple version of the authors' model suggests that—if the probability of having a child with Down syndrome were constant over maternal age—the expected utility from an amniocentesis is actually higher for younger women than for older women. Second, a more flexible version of the authors' model implies that amniocentesis rates, on average, should be higher for lower birth-order children, and that amniocentesis rates should decline as women reach the end of their reproductive period (Fahnzylber, et al., 2010).

Valerie Seror, however, claims that expected utility (EU) theory—which forms the basis of Fahnzylber, et al.'s model—is altogether a poor method for modeling a woman's optimal amniocentesis choice. In EU theory, potential outcomes are linearly weighted by the probability that each potential outcome occurs. Seror claims that this linear weighting fails to reveal a woman's optimal amniocentesis choice, because even though the probability of having a child with Down syndrome is incredibly low, the utility that a woman derives from a Down syndrome child is also quite low (or possibly negative). In particular, Seror questions EU theory's ability to model individuals' optimal choices when "all the probabilities associated with the outcomes are very high or very low…since the expected utilities of choice options are…highly insensitive to the utilities of outcomes." In the case of Down syndrome, Seror argues that EU theory suggests that women would favor the choice of 'no amniocentesis,' even though the valuable information provided by an amniocentesis suggests that, in reality, this may not be the case (Seror, 2008).

While not directly related to Down syndrome, Emily Oster, et al. find that individuals who are at-risk for Huntingdon's disease (HD) and who learn that they carry the gene that causes HD are significantly more likely to purchase long-term care insurance than individuals who are at-risk for HD but who learn that they do not carry the HD gene. Oster, et al.'s results imply that genetic testing can play a critical role in shaping an individual's healthcare decisions (Oster, et al., 2013).

My analysis seeks to fill in the gaps that exist in the current literature. To the best of my knowledge, I will be the first to explore the effects of an amniocentesis eligibility cutoff on women's choices and behavior in the U.S. Despite the fact that, for example, Ekelund, et al. find that the introduction of a national Down syndrome screening policy in Denmark significantly decreased both the number of invasive diagnostic procedures performed and the number of

babies born with Down syndrome, these results cannot easily be extrapolated to the U.S. After all, Denmark's homogenous demographic make-up and national health insurance scheme stand in sharp contrast to the U.S.' incredibly diverse population and private-market-driven healthcare system.

Furthermore, the vast majority of the relevant literature—and in particular, the relevant medical literature—simply documents overall time trends in diagnostic testing take-up and Down syndrome incidence. By centering my empirical strategy on the AMA amniocentesis eligibility cutoff, in any given year, I will be able to observe the choices and birth outcomes of both (1) AMA women who were offered an amniocentesis, and (2) non-AMA women who were not offered an amniocentesis. By using this additional level of difference to implement a RD design, I will be able to observe much more than broad changes in amniocentesis use and Down syndrome incidence over time: Rather, I will actually be able to establish a causal relationship between amniocentesis eligibility and women's amniocentesis take-up, and I will apply similar techniques to quantify the relationship between amniocentesis eligibility and corresponding birth outcomes.

Section 3: Data

To conduct my analysis, I utilize U.S. Vital Statistics live birth data from 1989 to 2002. Providing incredibly rich information on every documented U.S. live birth, Vital Statistics live birth data is publicly available through the Centers for Disease Control and Prevention (CDC). Over the course of 1989 to 2002, there were 60,137,858 recorded live births in the U.S. As will be explained in detail in the "Empirical Strategy" section of this paper, my analysis will focus only on first births, and in particular, on first births to mothers age 33 to 37, inclusive. Even

though I am limiting my sample to first births within a small neighborhood of the amniocentesis eligibility cutoff, the fact that the Vital Statistics data tracks the full universe of live births means that my preferred sample still captures the amniocentesis choices and birth outcomes of many AMA and non-AMA women.

At its core, Vital Statistics birth data is simply a compilation of the information recorded in the U.S. Standard Certificate of Live Birth, which—as its name aptly suggests—is completed after each live birth. In addition to providing a wealth of information regarding the health status of the newborn, this certificate also records the mother's prenatal care decisions and collects basic demographic information from both the mother and father. The period from 1989 to 2002 corresponds to the use of the 1989 revision of the U.S. Standard Certificate of Live Birth.

The 1989 revision of the U.S. Standard Certificate of Live Birth is the only version of the certificate that contains all of the information required for my empirical analysis. Critically, this version of the certificate records whether the baby has Down syndrome. Most importantly—and unlike previous or later versions of the certificate—the 1989 revision to the U.S. Standard Certificate of Live Birth explicitly asks mothers whether they underwent an amniocentesis. Given that my objective is to determine the effect that women's differential access to amniocentesis has on women's amniocentesis choices and subsequent birth outcomes, being able to track women's amniocentesis decisions is essential to the successful execution of my empirical strategy.

Table 1, which is given below, paints a basic descriptive picture of the mothers included in my dataset. In Column 1, the sample is restricted to first-time mothers who were between the ages of 33 and 37 (inclusive) at the time of the birth of their child (i.e., the sample is restricted to a two-year window around the AMA amniocentesis eligibility cutoff). As will be discussed in

more detail shortly, this restricted sample is my preferred sample for the remainder of my analysis, as comparing first-time mothers in a small neighborhood of the AMA amniocentesis eligibility cutoff will allow me to hone in on the causal effect of amniocentesis eligibility on amniocentesis take-up and birth outcomes.

Table 1 highlights several important differences between the sample of all first-time mothers and my preferred sample. In addition to being more likely, on average, to undergo an amniocentesis and give birth to a baby with Down syndrome, the sample of 33-year-old to 37-year-old first-time mothers were—perhaps unsurprisingly—substantially more likely to be married, to have a college degree, and to begin prenatal care in the first trimester. Moreover, the racial and ethnic composition differs substantially between the two samples: The fractions of Hispanic mothers and Hispanic fathers are nearly 50% smaller in my preferred sample, and the fraction of non-white mothers and fathers is also slightly smaller in the sample of 33-year-old to 37-year-old first-time mothers.

Table 1 also suggests that babies born to first-time mothers age 33 to 37 are, as a whole, less healthy than babies born to first-time mothers in my full sample. While the average linear five-minute Apgar score is nearly identical between the two samples, the probability that the baby's five-minute Apgar score is less than seven is actually seven percent higher in my preferred sample. (Babies with a five-minute Apgar score of at least seven are typically considered to be in good health.) Furthermore, the probabilities that the baby is born at a low birth weight ($<$2,500 grams and $\geq$1,500 grams) or very low birth weight ($<$1,500 grams) are 21% and 30% higher in my preferred sample, respectively. These statistics are not particularly surprising, however, given that older women's pregnancies are, in general, riskier than younger women's pregnancies (Kenny, et al., 2013).

Table 1, Summary Statistics: First-Time Mothers Age 33 to 37 vs. All First-Time Mothers (1989-2002 Combined)

	(1) *First-Time Mothers Age 33 to 37*	(2) *All First-Time Mothers (Age 18 to 45)*
Age	34.5706	25.4928
	(1.3587)	(5.4697)
Underwent an Amniocentesis	0.0990	0.0258
	(0.2986)	(0.1586)
Child was Born with Down syndrome	0.0006	0.0004
	(0.0248)	(0.0191)
Child's 5-Minute Apgar Score	8.8830	8.9062
	(0.8332)	(0.8116)
Child's 5-Minute Apgar Score <7	0.0135	0.0126
	(0.1152)	(0.1115)
Child was Born at a Low Birthweight (<2,500 g)	0.0739	0.0607
	(0.2615)	(0.2387)
Child was Born at a Very Low Birthweight (<1,500 g)	0.0185	0.0142
	(0.1349)	(0.1182)
Began Prenatal Care in the First Trimester	0.9250	0.8456
	(0.2634)	(0.3613)
Began Prenatal Care in the Second Trimester	0.0585	0.1228
	(0.2347)	(0.3282)
Began Prenatal Care in the Third Trimester	0.0111	0.0230
	(0.1046)	(0.1498)
Underwent an Ultrasound	0.6443	0.6253
	(0.4787)	(0.4840)
Non-white	0.1626	0.1870
	(0.3690)	(0.3900)
Hispanic	0.0861	0.1559
	(0.2804)	(0.3627)
Married	0.8672	0.6714
	(0.3393)	(0.4697)
Did Not Complete High School	0.0387	0.1437
	(0.1929)	(0.3508)
Graduated High School	0.2029	0.3540
	(0.4022)	(0.4782)
Completed Some College	0.2219	0.2363
	(0.4155)	(0.4248)
Graduated College	0.5365	0.2659
	(0.4987)	(0.4418)
Father's Age	35.8749	28.577
	(5.2211)	(6.3986)
Non-white Father	0.1437	0.1624
	(0.3508)	(0.3688)
Hispanic Father	0.0751	0.1549
	(0.2636)	(0.3618)
Sample Size	*1,897,912*	*20,364,357*

Standard deviations are given in parentheses. Each summary statistic except for father's age can be interpreted as the fraction of mothers in that sample who possess that particular characteristic.

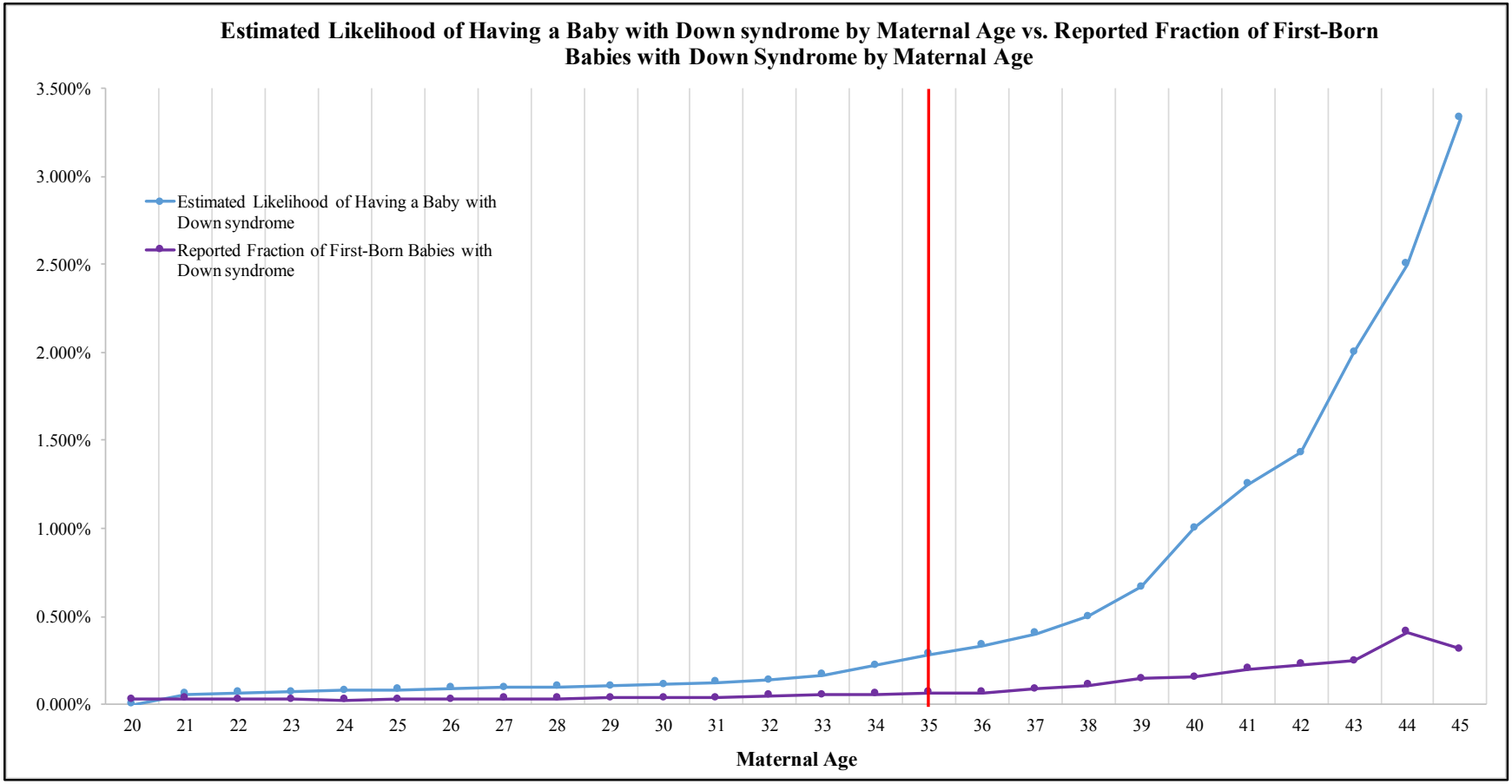
While not evident in Table 1, it is worth noting that there appears to be systematic underreporting of Down syndrome in the Vital Statistics data. In Figure 4, I have plotted the National Down Syndrome Society's estimates of the likelihood that the fetus will have Down syndrome against the reported fraction of babies born with Down syndrome at each maternal age. (The probabilities provided by the National Down Syndrome Society are consistent to those presented in the medical literature.) Given that this gap between predicted and reported Down syndrome incidence is stable around age 35 (where the amniocentesis eligibility cutoff is located), this apparent underreporting of Down syndrome in the Vital Statistics data should not jeopardize the validity of my empirical analysis, but it is concerning nevertheless.

There are several possible explanations for this gap. First, it may be the case that the estimates given in the medical literature are inaccurate. My background research suggests that these probabilities were calculated in the 1970s, when doctors and scientists—with the help of modern technology—were only first beginning to develop a detailed understanding of Down syndrome. Second, this apparent reporting gap may be reflective of women terminating pregnancies where a prenatal genetic test reveals that the fetus has Down syndrome. As I discuss in the "Main Results" section of this paper, however, I find no evidence that this is the case.

Third, it is my understanding that the estimated probabilities of having a child with Down syndrome that are presented in the medical literature attempt to capture the underlying biological risk that the fetus will *develop* Down syndrome upon conception (i.e., that meiotic nondisjunction will occur). Since pregnancies in which the fetus develops Down syndrome have a substantially elevated risk for spontaneous termination, it is possible that a portion of this reporting gap in Down syndrome is due to the fact that some fetuses with Down syndrome spontaneously abort prior to birth (Morris, et al., 1999). Finally, it is possible that—at least in

some cases—Down syndrome may not be detected in time to be recorded on the birth certificate. Babies with Down syndrome typically suffer from other health problems (like congenital heart defects) that often require immediate care after birth. If doctors are primarily concerned with other health problems, they may not test for Down syndrome in time for it to be included in the information provided on the birth certificate.

Figure 4

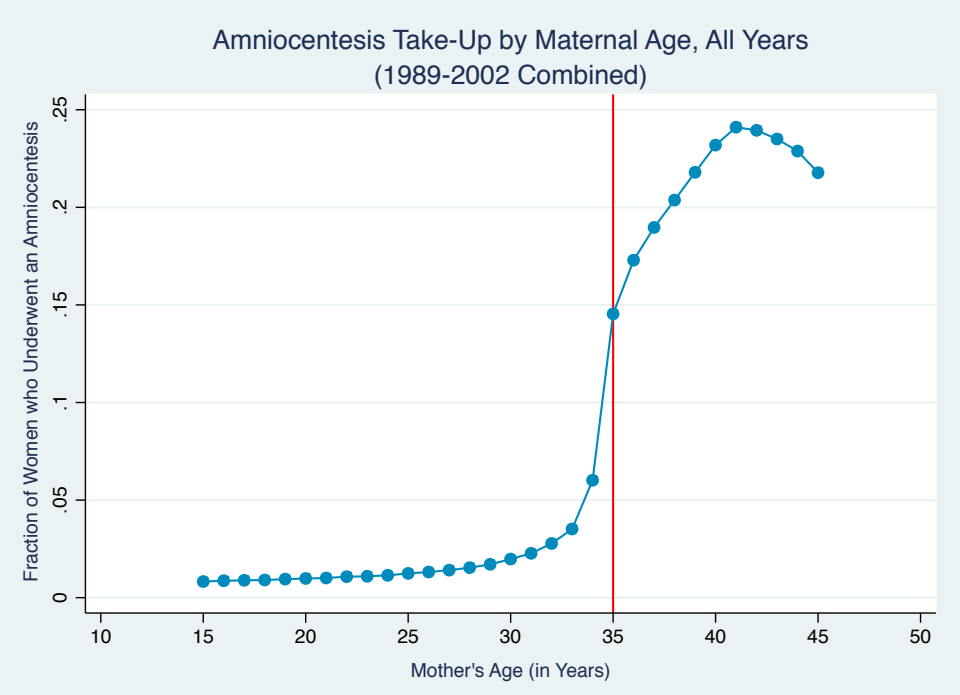


Sources: National Down syndrome Society (blue line) and Vital Statistics Birth Data from 1989 to 2002 (purple line)

Section 4: Descriptive Results

Before outlining my empirical strategy, I will first present graphical evidence that becoming eligible for an amniocentesis did—in fact—have a substantial impact on women's prenatal testing decisions. In Figure 5, I plot the fraction of women who underwent an amniocentesis by maternal age over the combined period from 1989 to 2002. Displaying a sharp "jump" in amniocentesis take-up at age 35 (the amniocentesis eligibility cutoff) of around seven percentage points, Figure 5 provides strong evidence that there is a positive discontinuity in the probability that a woman undergoes an amniocentesis at age 35.

Figure 5



Instead of pooling all of the years in my sample together, Figure 6 graphs the fraction of women who underwent an amniocentesis by maternal age separately for each year from 1989 to 2002. While there is a noticeable increase in the fraction of women who undergo an amniocentesis at age 35 in each year of the sample, the size of this discontinuity is monotonically decreasing over time. This clear downward trend in the fraction of women undergoing an amniocentesis at age 35 seems to suggest that amniocentesis-eligible women substituted away from amniocentesis as new, safer prenatal screening tests for Down syndrome became available.

Figure 6

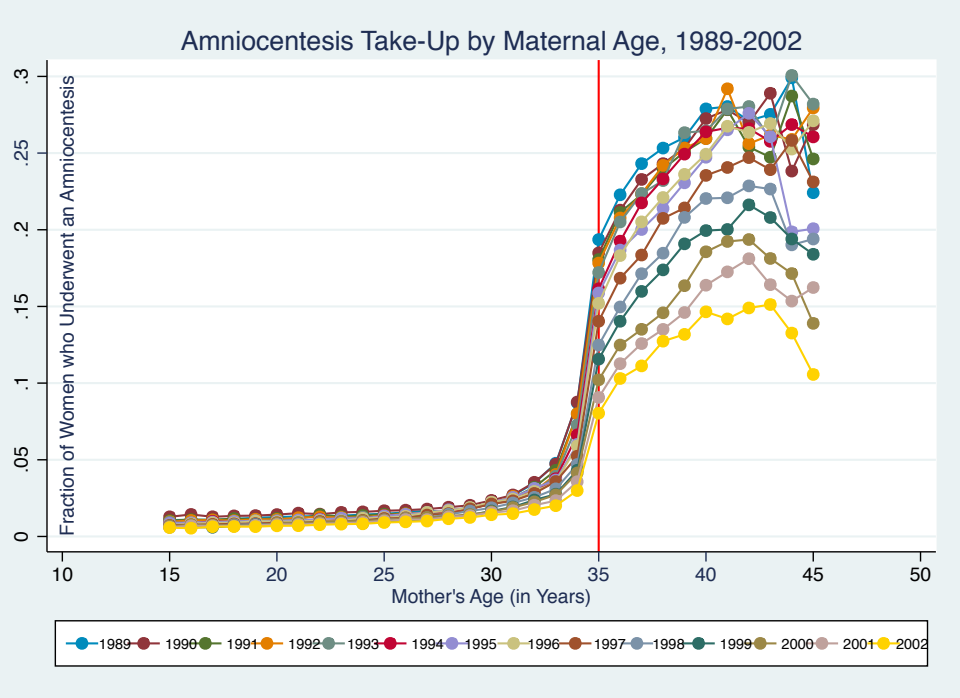
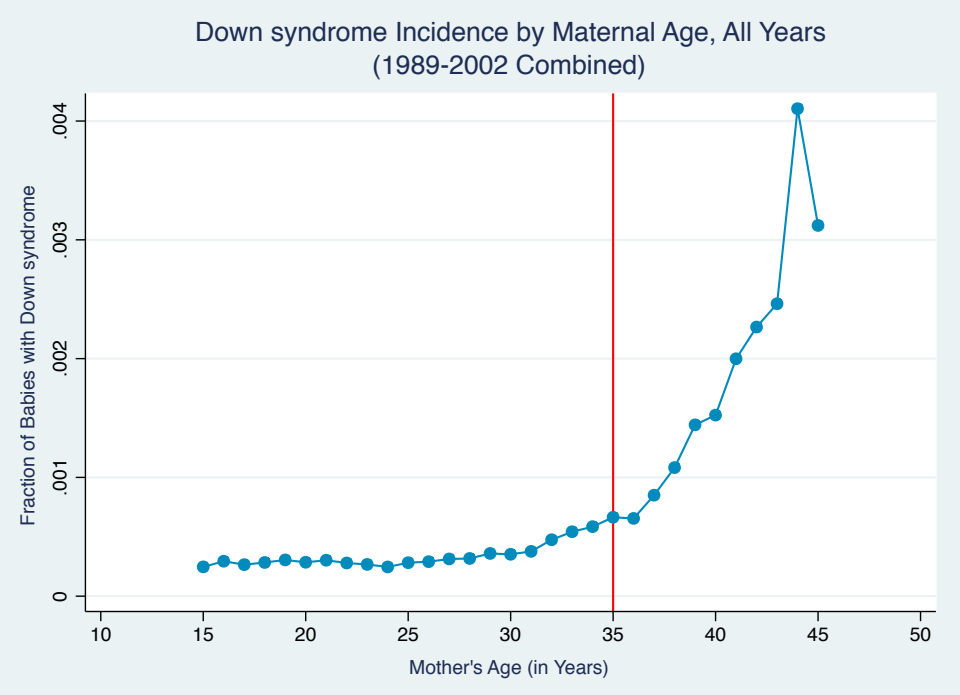


Figure 7 depicts the fraction of babies born with Down syndrome by maternal age over the period from 1989 to 2002. Given that the probability of having a child with Down syndrome rises with maternal age, a noticeable decrease in Down syndrome incidence at age 35 would imply that a substantial fraction of women acted on their amniocentesis results by terminating pregnancies in which the fetus was revealed to have Down syndrome. Interestingly, however, in Figure 7, there is no apparent break in the fraction of babies born with Down syndrome at age 35. It is important to note, however, that the lack of a readily-visible discontinuity in Down syndrome incidence at the AMA amniocentesis eligibility threshold is not enough to simply dismiss the possibility of a link between amniocentesis eligibility and Down syndrome incidence. Determining whether such a relationship exists will require a more thorough econometric analysis.

Figure 7



Section 5: Empirical Strategy

The sharp increase in amniocentesis take-up at the AMA amniocentesis eligibility threshold lends itself nicely to a Regression Discontinuity (RD) design. Explained simply, RD is an empirical method that can be used to estimate the causal effect of a treatment when access to the treatment is determined by an arbitrary cutoff. More formally, RD is typically an appropriate econometric technique when an individual only receives the treatment—or at the very least, only receives *access* to the treatment—when her value of an observed "assignment variable" (denoted here by X) exceeds that of some cutoff (denoted here by c).

The intuition behind RD is easily digestible. If the cutoff that determines access to a treatment is entirely arbitrary and individuals cannot *precisely* manipulate the assignment variable X, then individuals whose value of X was just high (or low) enough to qualify them for a particular treatment are likely not fundamentally different from individuals whose value of X fell just short of the cutoff, *except* for the fact that individuals who qualified for the treatment actually received (or became eligible for) the treatment. If this is the case, then any variation in treatment status around the cutoff can be considered as good as randomly assigned. For a "sharp" RD—where the probability of receiving treatment jumps from 0 to 1 at the threshold c—this means that any variation in outcomes around the cutoff can be interpreted as the causal effect of the treatment.

For my empirical analysis, I will employ a variant of a "fuzzy" RD design. Unlike a sharp RD, a fuzzy RD does not require treatment assignment to be a deterministic function of X. Instead, a fuzzy RD allows the discontinuity in the probability of treatment at the cutoff $X = c$ to be less than one. Formally, this discontinuity condition can be stated as:

$$\lim_{\epsilon \downarrow 0} Pr[T_i = 1 |\ X_i = c + \varepsilon] \neq \lim_{\epsilon \uparrow 0} Pr[T_i = 1 |\ X_i = c + \varepsilon]$$

where T_i is an indicator variable that equals one when an individual receives treatment and zero otherwise.

I will use RD to exploit the fact that the amniocentesis eligibility threshold at age 35 is arbitrary. To calculate the causal effect of amniocentesis access on amniocentesis take-up and birth outcomes, I will effectively be comparing the amniocentesis use and birth outcomes of women just over the age of 35 (who were offered an amniocentesis) to women just under the age of 35 (who did not qualify for an amniocentesis).

In order for RD to be an appropriate econometric technique, however, several conditions must hold. Perhaps most importantly, an RD design requires that individuals are unable to precisely manipulate the assignment variable X, which in this context is the mother's age at the birth of her child. Considering that, as of 2013, 61.7% of women aged 15 to 44 were actively using some form of contraception, it is possible that some women delayed having children until they were at least 35, in order to ensure access to an amniocentesis (CDC, 2014). It is unlikely, however, that women were able to *precisely* manipulate their age at the birth of their child, particularly in the neighborhood of the AMA amniocentesis eligibility threshold. While modern contraceptives can be used to help avoid an unplanned pregnancy, it is highly unlikely that a woman will become pregnant immediately after she stops using contraceptives. Exactly when a woman will become pregnant after she stops using contraceptives is uncertain, and this uncertainty rises with maternal age (American Pregnancy Association, 2017).

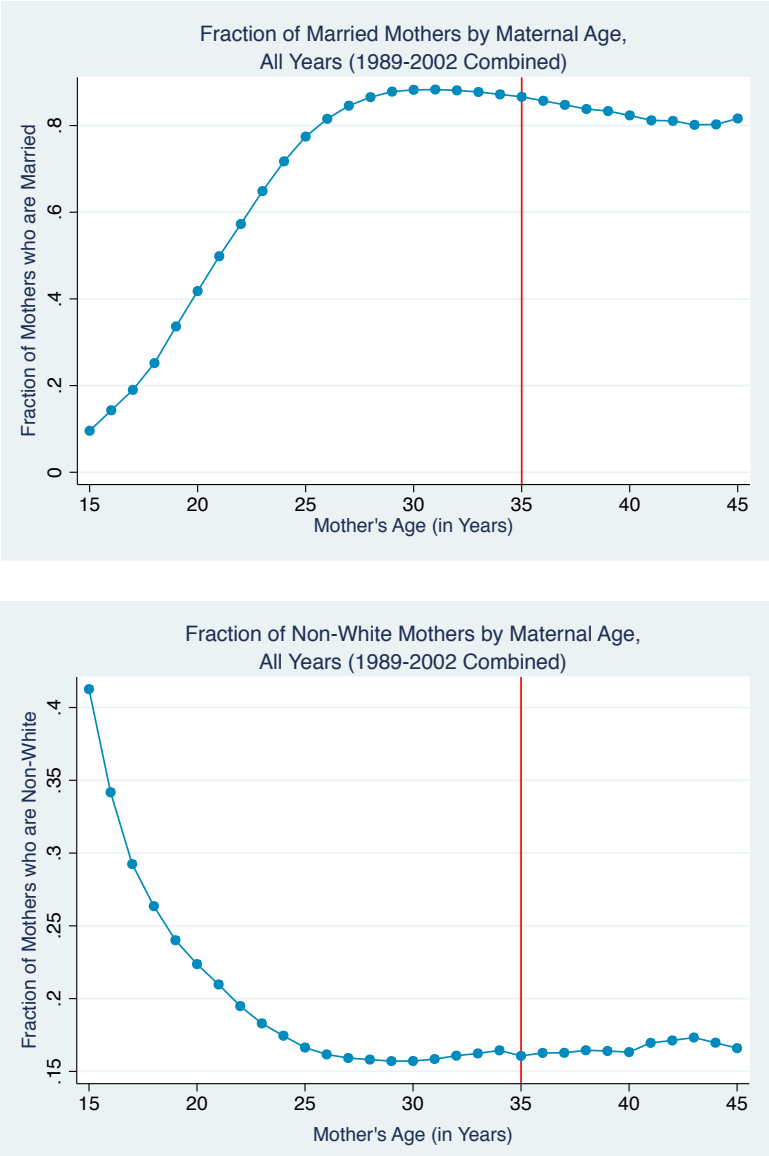
Additionally, in order for women near the AMA amniocentesis eligibility threshold to even have had an incentive to precisely manipulate the age at which they gave birth, it must be the case that women were aware of the AMA amniocentesis eligibility cutoff *before* they became pregnant. While the AMA amniocentesis eligibility cutoff was a nationally adopted practice, it was not explicitly publicized to women who were contemplating becoming pregnant, building my confidence in my assumption that there is not differential sorting across the AMA amniocentesis eligibility threshold. As a cautionary step, however, I limit my analysis to first-time mothers, as first-time mothers were likely the least aware of the AMA eligibility cutoff prior to becoming pregnant.[8]

To empirically test whether there is differential sorting across the AMA threshold, I conducted "placebo RDs" on several covariates that were determined prior to treatment assignment, such as the mother and father's race and ethnicity. In Figure 8, I plot the mean value of these characteristics by maternal age for all first-time mothers over the entire period from 1989 to 2002. Reassuringly, there does not appear to be a "jump" in any of these baseline characteristics at the AMA amniocentesis eligibility cutoff, increasing my confidence that the only systematic difference between AMA women and non-AMA women is amniocentesis eligibility. To ensure that these results were not solely a function of convenient scaling of my y-axes, I also estimated equation (1) (described below) separately for each baseline characteristic over the period from 1989-2002 combined, using the baseline characteristic as the dependent

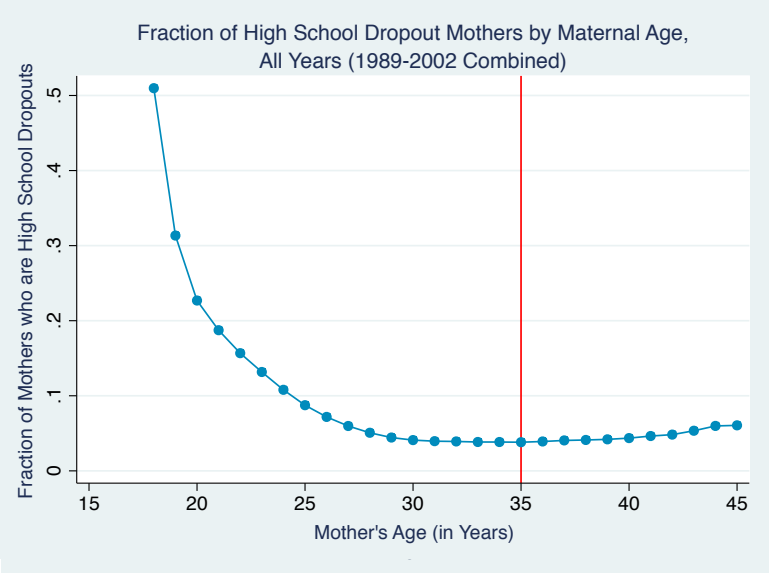
[8] While not featured in this paper, I also repeated my analysis with second-births, and my results were broadly consistent with my results from my analysis of first-births.

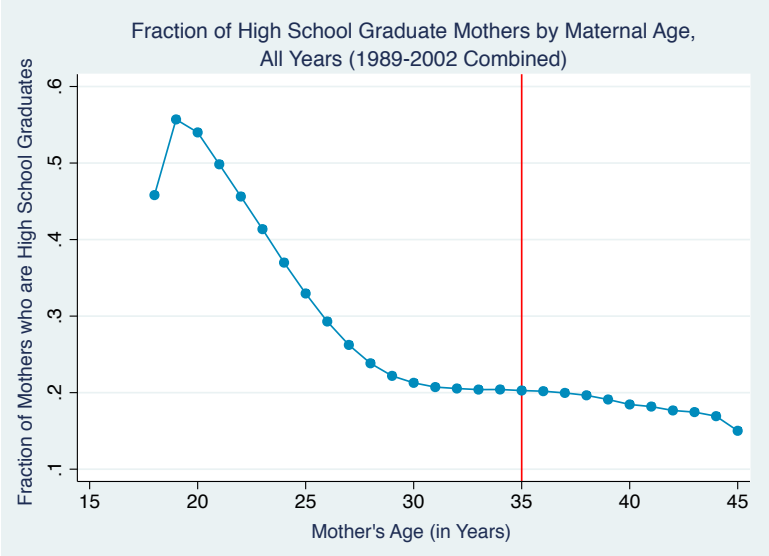
variable. Consistent with the pictures painted in Figure 8, the results from this set of regressions are given in the appendix.[9]

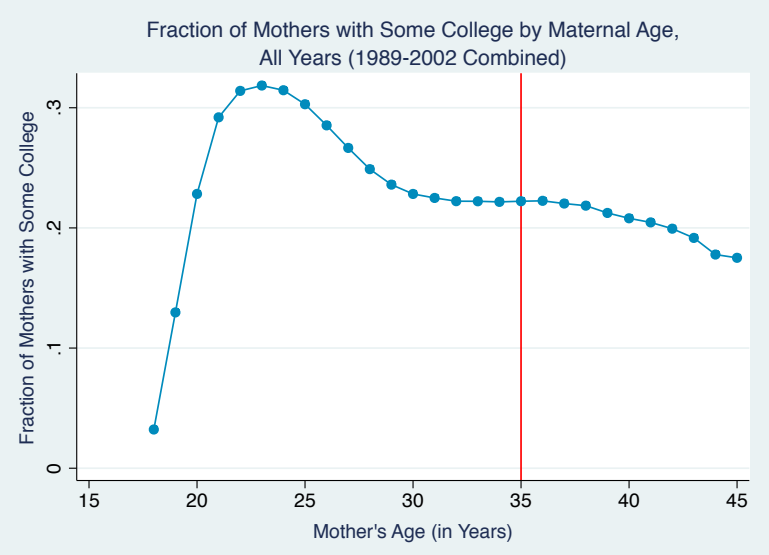
Figure 8

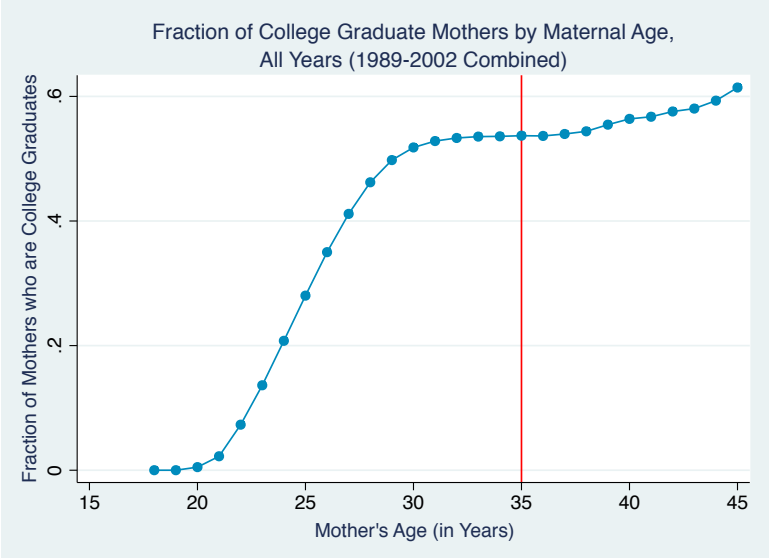


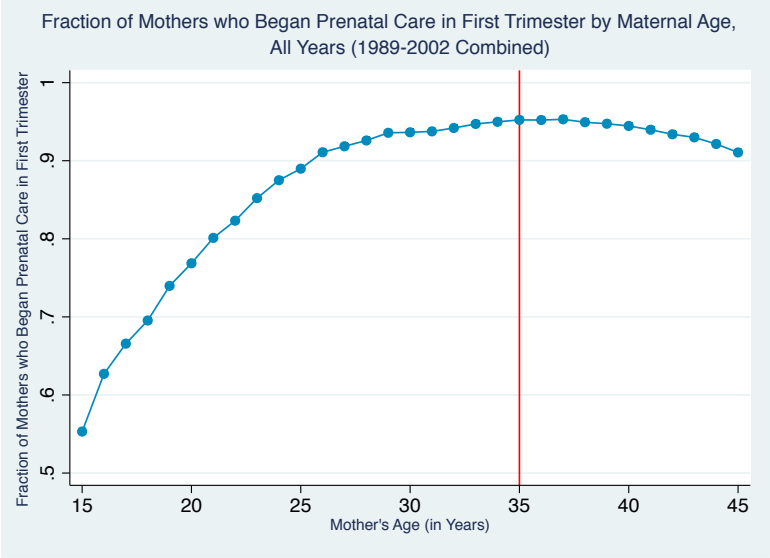
[9] While several of the regression coefficients of interest are statistically significant at the five percent level, the point estimates are quite small relative to the mean, arguably rendering these results economically insignificant.

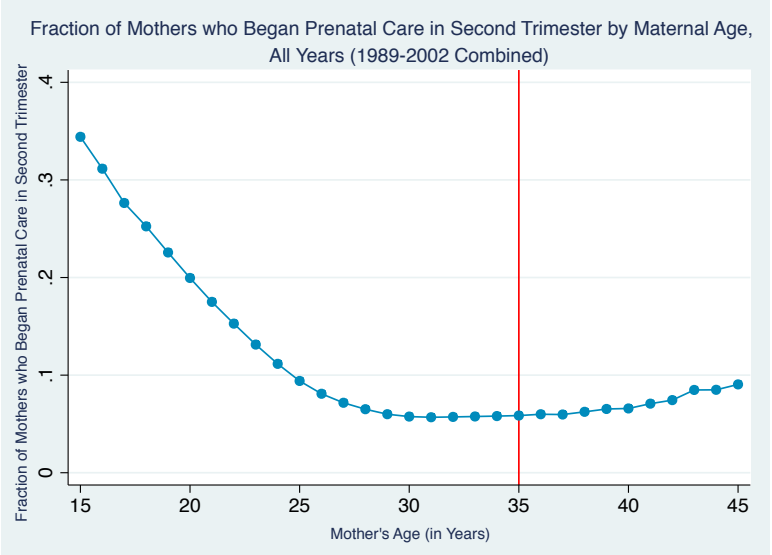

Fraction of High School Dropout Mothers by Maternal Age,
All Years (1989-2002 Combined)
Fraction of Mothers who are High School Dropouts
0
.1
.2
.3
.4
.5
15
20
25
30
35
40
45
Mother's Age (in Years)

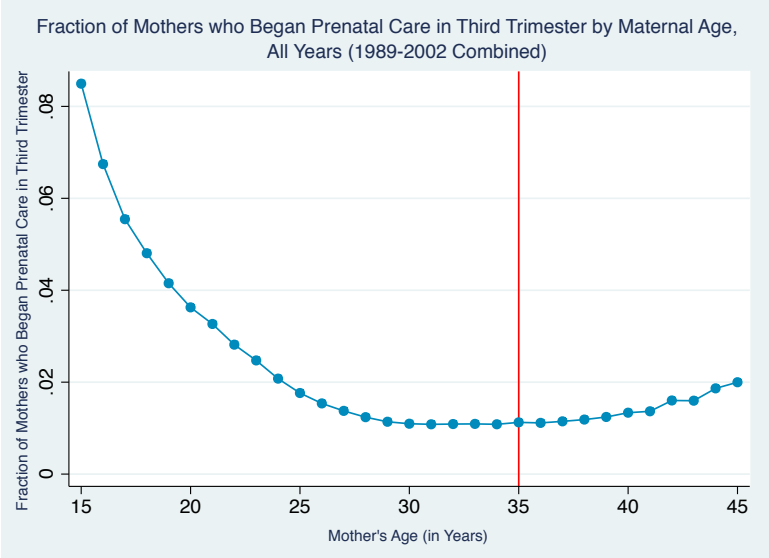

Fraction of High School Graduate Mothers by Maternal Age,
All Years (1989-2002 Combined)
Fraction of Mothers who are High School Graduates
.1
.2
.3
.4
.5
.6
15
20
25
30
35
40
45
Mother's Age (in Years)

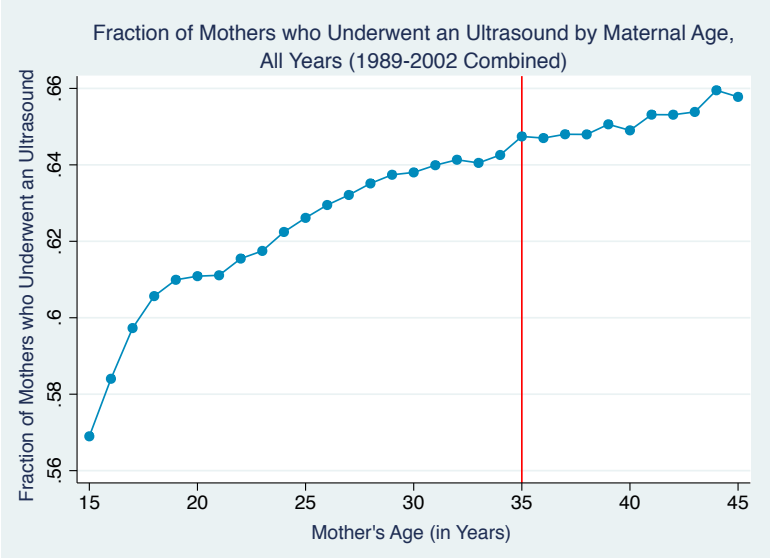

Fraction of Mothers with Some College by Maternal Age,
All Years (1989-2002 Combined)
Fraction of Mothers with Some College
0
.1
.2
.3
15
20
25
30
35
40
45
Mother's Age (in Years)

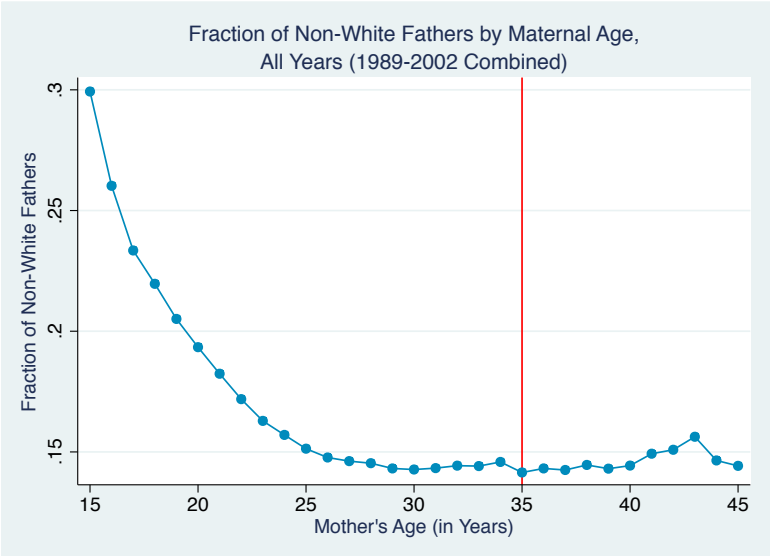

Fraction of College Graduate Mothers by Maternal Age,
All Years (1989-2002 Combined)
Fraction of Mothers who are College Graduates
0
.2
.4
.6
15
20
25
30
35
40
45
Mother's Age (in Years)

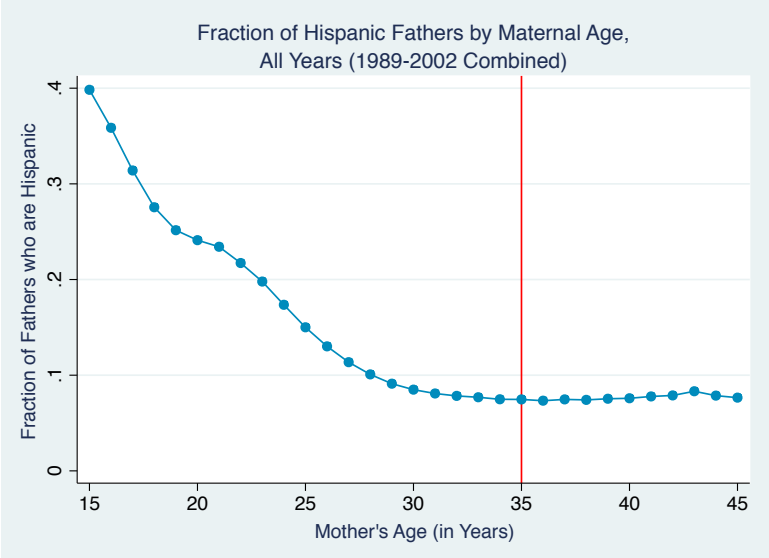

Fraction of Mothers who Began Prenatal Care in First Trimester by Maternal Age,
All Years (1989-2002 Combined)
Fraction of Mothers who Began Prenatal Care in First Trimester
.5
.6
.7
.8
.9
1
15
20
25
30
35
40
45
Mother's Age (in Years)


Fraction of Mothers who Began Prenatal Care in Second Trimester by Maternal Age,
All Years (1989-2002 Combined)
Fraction of Mothers who Began Prenatal Care in Second Trimester
0
.1
.2
.3
.4
15
20
25
30
35
40
45
Mother's Age (in Years)


Fraction of Mothers who Began Prenatal Care in Third Trimester by Maternal Age, All Years (1989-2002 Combined)
Fraction of Mothers who Began Prenatal Care in Third Trimester
0
.02
.04
.06
.08
15
20
25
30
35
40
45
Mother's Age (in Years)


Fraction of Mothers who Underwent an Ultrasound by Maternal Age, All Years (1989-2002 Combined)
Fraction of Mothers who Underwent an Ultrasound
.56
.58
.6
.62
.64
.66
15
20
25
30
35
40
45
Mother's Age (in Years)


Fraction of Non-White Fathers by Maternal Age, All Years (1989-2002 Combined)
Fraction of Non-White Fathers
.15
.2
.25
.3
15
20
25
30
35
40
45
Mother's Age (in Years)



Lastly, in order for an RD design to be an appropriate empirical design, it must also be true that there are no other relevant changes at age 35 that could influence amniocentesis take-up or birth outcomes (or both). To the best of my knowledge, no other medical procedures or guidelines employ 35 as an eligibility cutoff. Furthermore, even though the probability that a woman will have a child with Down syndrome increases with maternal age, this increase is continuous and gently rolls across the AMA threshold, suggesting that there is not a sudden biological difference between AMA and non-AMA women located close to the amniocentesis eligibility threshold. As the blue line in Figure 4 shows, the medical literature's estimates of the probability of having a child with Down syndrome does not suddenly increase at the age of 35. (Figure 4 is displayed in the "Data" section of this paper.)

To actually implement an RD design and quantify the discontinuity in amniocentesis take-up at the AMA eligibility cutoff, I estimate local linear regressions. The basic regression model that I will use to non-parametrically estimate the size of this discontinuity is as follows:

$$\textbf{(1)}\ A_{it} = \alpha + \delta_A \mathbf{1}(X_{it} - 35 \geq 0) + \gamma(X_{it} - 35) + \lambda(X_{it} - 35) * \mathbf{1}(X_{it} - 35 \geq 0) + W_{it}\beta' + \varepsilon_{it}$$

where A_{it} is an indicator variable that equals one if woman *i* undergoes an amniocentesis in year t, X_{it} is woman *i*'s age at the birth of her child, $\mathbf{1}(X_{it} - 35 \geq 0)$ is an indicator variable that equals one when a woman is 35 or older (and therefore qualifies for an amniocentesis), $(X_{it} - 35)$ is a linear function (centered at age 35) that describes the relationship between a woman's age at birth and the probability that she undergoes an amniocentesis, and W_{it} is a vector of other controls.[10] (For the remainder of the paper, I will refer to the variable $\mathbf{1}(X_{it} - 35 \geq 0)$ simply as *AMA*.) Normalizing the assignment variable to zero at the cutoff $c = 35$ allows me to interpret $\hat{\delta}_A$ as the size of the discontinuity in amniocentesis use at age 35, and the interaction term $(X_{it} - 35) * \mathbf{1}(X_{it} - 35 \geq 0)$ allows the relationship between maternal age and amniocentesis use to differ on both sides of the cutoff.

Since equation (1) is a local linear regression, my first challenge was to select the "optimal" bandwidth for the regression. At its core, the bandwidth selection problem boils down to a tradeoff between precision and bias. On the one hand, a narrow bandwidth ensures that a line will be a better approximation for the underlying relationship between the assignment variable and the outcome variable, but a narrow bandwidth utilizes observations from only a small portion of the overall sample, reducing the precision of the estimates. Conversely, a wide bandwidth will provide more precise estimates, but it will also likely be more biased, as a line will probably be a poor fit for data far away from the cutoff.

[10] It is worth noting that a sharp RD is just a special case of a fuzzy RD, where $\delta_A = 1$ and all other regression coefficients equal zero.

I calculated the "optimal" bandwidth for my local linear regression by following the procedure recommended by Guido Imbens and Karthik Kalyanaraman (Imbens and Kalyanaraman, 2012). When applied to my dataset, the Imbens and Kalyanaraman (IK) bandwidth selection method recommends a bandwidth of approximately 1.09.[11] Unfortunately, my assignment variable—a woman's age at the birth of her child—is discrete, in the sense the Vital Statistics birth data measures maternal age in one-year intervals. This "lumping" of the assignment variable renders it impossible for me to utilize a bandwidth of exactly 1.09. As a result, my preferred bandwidth is two, and the results presented in the body of this paper will feature regressions implemented with a bandwidth of two. Importantly, however, my results are qualitatively consistent with a host of bandwidths, ranging from three to ten, and these alternative sets of results are given in the "Robustness Checks and Falsification Tests" section of the paper.

I first estimate equation (1) with a bandwidth of two around the AMA threshold over the entire period from 1989 to 2002, in order to calculate the "average" effect of amniocentesis eligibility on amniocentesis take-up. (My regression estimations with a bandwidth of two only include first-time mothers age 33 to 37, inclusive.) Then, in order to track whether the size of the discontinuity in amniocentesis use at the AMA threshold varied over time with the introduction of screening tests for Down syndrome, I estimate equation (1) separately for each of the years from 1989 to 2002.

[11] While I was unable to estimate the optimal bandwidth using my full sample, the optimal bandwidth for a 20% random sample of my data was 1.09. Furthermore, when I estimated the optimal bandwidth for each year from 1989 to 2002, the range of optimal bandwidths was 1.22 to 1.37, providing me with more confidence that the optimal bandwidth for my full sample would be between one and two.

After quantifying the effect of amniocentesis eligibility on amniocentesis use, I explore whether there is a corresponding discontinuity in Down syndrome incidence at the AMA threshold. That is, I directly estimate the effect of amniocentesis eligibility on Down syndrome incidence. Also estimated using a bandwidth of two years, this "reduced form" regression model is given as follows:

$$\textbf{(2)}\ DS_{it} = \alpha + \delta_{DS}\mathbf{1}(X_{it} - 35 \geq 0) + \gamma(X_{it} - 35) + \lambda(X_{it} - 35) * \mathbf{1}(X_{it} - 35 \geq 0) + W_{it}\beta' + \varepsilon_i$$

where DS_{it} is an indicator variable that equals one if woman *i*'s child has Down syndrome. (All other variables and subscripts are identical to those in equation (1).) Similar to equation (1), $\hat{\delta}_{DS}$ is my coefficient of interest. Considering the estimated biological probability of having a child with Down syndrome rises with maternal age (see Figure 4), if a substantial fraction of women who underwent an amniocentesis terminated pregnancies where the fetus tested positive for Down syndrome, I would expect the estimated coefficient $\widehat{\delta_{DS}}$ to be negative. My main results are given in the next section.

Section 6: Main Results

The Effect of Amniocentesis Eligibility on Amniocentesis Take-Up

Table 2 presents the results from the implementation of regression equation (1) with a bandwidth of two (that is, using first-time mothers age 33 to 37), for all my data years (1989-2002) combined. Column 1 does not include any controls, and Column 2 includes controls for a vector of seven maternal and paternal baseline characteristics. Reassuringly, the point estimate of interest (the estimated coefficient on *AMA*) is robust to the inclusion of these controls, providing

additional evidence that there was not differential sorting across the AMA amniocentesis eligibility threshold. The estimated coefficient on *AMA* in Column 2 of Table 2 implies that the probability a woman underwent an amniocentesis increased by 6.17 percentage points at the AMA amniocentesis eligibility threshold, a 62% increase over the mean amniocentesis take-up rate for 33 to 37 year-olds, and a staggering 239% increase over the mean amniocentesis take-up for the entire sample of first-time mothers. This coefficient—which is my key coefficient on interest—is statistically significant at the one-percent level. Since in Table 2, equation (1) was estimated using all of my data years combined, the estimated coefficients on *AMA* can be interpreted as the average effect of amniocentesis eligibility on amniocentesis take-up across my entire sample period (1989-2002).

In Column 3, I add year fixed effects, and in Column 4, I add an indicator variable that equals one if the year is at least 1996, and I interact this dummy variable with *AMA*, *Age – 35*, and *(Age – 35)*AMA*. In 1996, the quadruple screen was introduced, and it was arguably the most important new prenatal screening test introduced over my sample period (1989-2002). (The quadruple screen was still the most popular screening test for Down syndrome in 2011, the latest year for which information on screening test take-up is available (Palomaki, et al., 2013).) Moreover, as seen in Figure 1, the use of *all* screening tests (including the previously-introduced triple screen) increased dramatically in the early 1990s, suggesting that the use of amniocentesis might have been different in the first and second half of this decade. Thus, the interaction term between *Post-1996* and *AMA* provides a rough estimate of the extent to which AMA women's amniocentesis testing decisions changed in response to the introduction of new screening tests for Down syndrome.

As I briefly discussed in the "Background" section of this paper, the effect of the availability of these new screening tests on amniocentesis take-up is theoretically ambiguous. On the one hand, unlike an amniocentesis, screening tests for Down syndrome present essentially zero risk to the fetus, and this reduction in risk may have led AMA women to substitute away from amniocentesis as new prenatal screening tests became available. On the other hand, it is possible that the introduction of screening tests actually increased amniocentesis use among AMA women. That is, these new screening tests may have induced a new "type" of woman to undergo an amniocentesis—namely, women who were concerned about the risks surrounding an amniocentesis and only underwent an amniocentesis because they received a positive result on a screening test for Down syndrome. My results are consistent with the first story, as the point estimate on *Post-1996*AMA* implies that 35-year-old women who gave birth to their first child in 1996 or later were one percentage point (or 10%) less likely to undergo an amniocentesis than 35-year-old women who gave birth to their first child prior to 1996.

Table 2, The Effect of Amniocentesis Eligibility on Amniocentesis Take-Up, All Years (1989-2002 Combined)

	(1)	(2)	(3)	(4)
AMA	0.0619***	0.0617***	0.0620***	0.0680***
	(0.0018)	(0.0018)	(0.0018)	(0.0020)
Age – 35	0.0237***	0.0228***	0.0229***	0.0329***
	(0.0000)	(0.0001)	(0.0001)	(0.0002)
(Age – 35)*AMA	-0.0020	-0.0019	-0.0016	-0.0097***
	(0.0015)	(0.0015)	(0.0015)	(0.0018)
Post-1996				-0.0346***
				(0.0064)
(Post-1996)*AMA				-0.0100***
				(0.0005)
(Post-1996)*(Age – 35)				-0.0184***
				(0.0001)
(Post-1996)*(Age – 35)*AMA				0.0154***
				(0.0005)
Non-white Mother		-0.0123**	-0.0096*	-0.0096*
		(0.0044)	(0.0038)	(0.0038)
Hispanic Mother		-0.0176**	-0.0137**	-0.0137**
		(0.0057)	(0.0047)	(0.0047)
Mother Did Not Complete High School		-0.0238*	-0.0247*	-0.0248*
		(0.0095)	(0.0100)	(0.0100)
Mother Completed Some College		0.0134**	0.0149**	0.0147**
		(0.0047)	(0.0049)	(0.0049)
Mother Graduated College		0.0337**	0.0382**	0.0377**
		(0.0093)	(0.0100)	(0.0101)
Mother is Married		-0.0057***	-0.0056***	-0.0055***
		(0.0009)	(0.0007)	(0.0007)
Father's Age		0.0011***	0.0012***	0.0012***
		(0.0002)	(0.0002)	(0.0002)
Non-white Father		-0.0195**	-0.0193**	-0.0193**
		(0.0053)	(0.0052)	(0.0052)
Hispanic Father		-0.0178**	-0.0157**	-0.0158**
		(0.0053)	(0.0047)	(0.0047)
Constant	0.0813***	0.0326**	0.0588***	0.0640***
	(0.0000)	(0.0088)	(0.0025)	(0.0086)
Year Fixed Effects	No	No	Yes	Yes
Mean of Dependent Variable	*0.0990*	*0.0990*	*0.0990*	*0.0990*
N	*1,679,707*	*1,679,707*	*1,679,707*	*1,679,707*
R^2	*0.0404*	*0.0462*	*0.0531*	*0.0544*

The dependent variable is an indicator variable that equals one if the mother underwent an amniocentesis. All regressions were estimated using a bandwidth of two (i.e., only first-time mothers ages 33 to 37 (inclusive) were included in the sample). AMA is an indicator variable that equals one if the mother was at least age 35 at the birth of her child, and Post-1996 is an indicator variable that equals one if the year is at least 1996. Standard errors are clustered by mother's age, and standard errors are given in parentheses.

$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

To more precisely estimate the extent to which the discontinuity in amniocentesis take-up at the AMA threshold evolved over my sample period, I next estimate equation (1) separately for each data year from 1989 to 2002. Since the amniocentesis eligibility cutoff remained at 35 over my entire sample period, any decline in amniocentesis take-up at age 35 is likely caused by women substituting away from amniocentesis and towards prenatal screening tests for Down syndrome.

In each of the regression estimations, I include the same vector of controls seen in Table 2, and I restrict the bandwidth to two. Table 3 presents the results from these regressions, and the $\hat{\delta}_A$'s (the point estimates of interest) are depicted graphically in Figure 9.

Although the point estimates on *AMA* bounce around in magnitude from 1989 to the mid 1990s, the size of the estimated discontinuity in amniocentesis take-up at the AMA threshold begins to shrink in the late 1990s, and this downward trend continues until 2002, the final year in my dataset. In 1989, for example, my results suggest that the probability a woman underwent an amniocentesis increased by 6.84 percentage points at the amniocentesis eligibility cutoff, but the size of this discontinuity had shrunk to 4.35 percentage points by 2002, a 36% decline. This negative trend in the second half of my sample period is quite visible in Figure 9.

Table 3, The Effect of Amniocentesis Eligibility on Amniocentesis Take-Up, Estimated Separately for 1989-2002

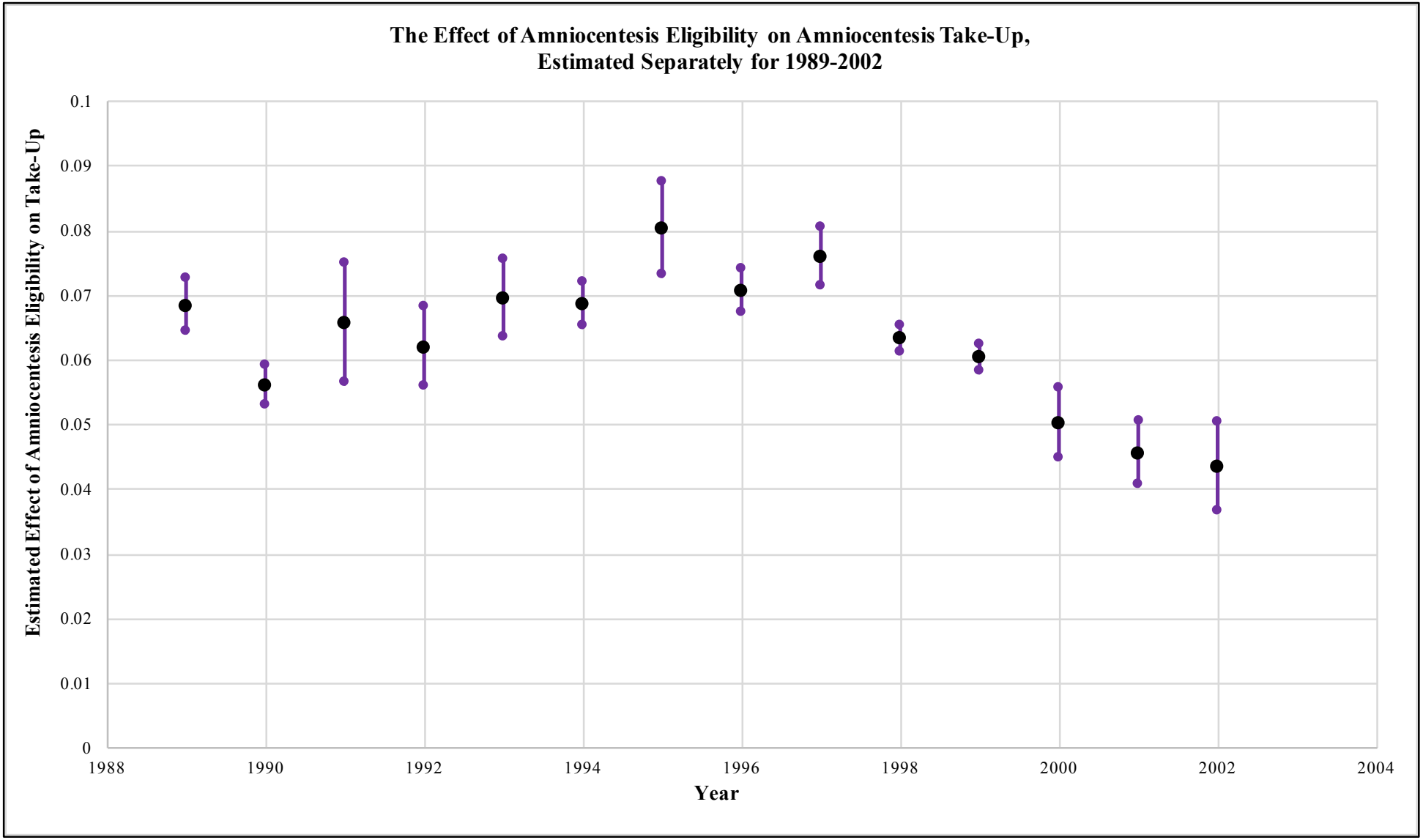
	(1) 1989	(2) 1990	(3) 1991	(4) 1992	(5) 1993	(6) 1994	(7) 1995
AMA	0.0684***	0.0561***	0.0656***	0.0620***	0.0696***	0.0686***	0.0803***
	(0.0015)	(0.0011)	(0.0033)	(0.0022)	(0.0022)	(0.0012)	(0.0026)
Age – 35	0.0382***	0.0392***	0.0360***	0.0390***	0.0323***	0.0294***	0.0228***
	(0.0001)	(0.0002)	(0.0001)	(0.0003)	(0.0002)	(0.0001)	(0.0001)
(Age – 35)*AMA	-0.0164***	-0.0167***	-0.0156***	-0.0160***	-0.0063**	-0.0009	-0.0019
	(0.0014)	(0.0010)	(0.0030)	(0.0019)	(0.0019)	(0.0011)	(0.0023)
Constant	0.0833***	0.0768***	0.0810***	0.0751***	0.0674***	0.0710***	0.0558***
	(0.0059)	(0.0131)	(0.0079)	(0.0145)	(0.0101)	(0.0042)	(0.0071)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mean of Dependent Variable	*0.1083*	*0.1281*	*0.1238*	*0.1228*	*0.1200*	*0.1130*	*0.1083*
N	*83,893*	*93,752*	*101,444*	*108,474*	*112,122*	*119,393*	*121,624*
R^2	*0.0603*	*0.0545*	*0.0564*	*0.0586*	*0.0605*	*0.0583*	*0.0553*

	(8) 1996	(9) 1997	(10) 1998	(11) 1999	(12) 2000	(13) 2001	(14) 2002
AMA	0.0707***	0.0759***	0.0632***	0.0603***	0.0502***	0.0456***	0.0435***
	(0.0012)	(0.0017)	(0.0007)	(0.0008)	(0.0019)	(0.0018)	(0.0025)
Age – 35	0.0232***	0.0157***	0.0160***	0.0146***	0.0142***	0.0123***	0.0101***
	(0.0002)	(0.0002)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)
(Age – 35)*AMA	0.0042**	0.0060**	0.0069***	0.0082***	0.0030	0.0056**	0.0067**
	(0.0011)	(0.0014)	(0.0007)	(0.0006)	(0.0017)	(0.0015)	(0.0021)
Constant	0.0555***	0.0255**	0.0198*	0.0173	0.0155	0.0199*	0.0129
	(0.0112)	(0.0092)	(0.0091)	(0.0107)	(0.0113)	(0.0076)	(0.0098)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mean of Dependent Variable	*0.1069*	*0.0986*	*0.0891*	*0.0836*	*0.0740*	*0.0659*	*0.0575*
N	*126,503*	*130,198*	*132,951*	*133,656*	*138,893*	*140,670*	*145,509*
R^2	*0.0551*	*0.0480*	*0.0435*	*0.0411*	*0.0333*	*0.0313*	*0.0295*

The dependent variable is an indicator variable that equals one if the mother underwent an amniocentesis. All regressions were estimated using a bandwidth of two (i.e., only first-time mothers ages 33 to 37 (inclusive) were included in the sample). All regressions include controls for the mother and father's race and ethnicity, the mother's marital status, and the mother's educational attainment. AMA is an indicator variable that equals one if the mother was at least 35 at the birth of her child. Standard errors are clustered by mother's age, and standard errors are given in parentheses.

$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

Figure 9



Note: 95% confidence intervals are given in purple

Interpreted at its most simplistic level, this significant decrease in the size of the discontinuity in amniocentesis take-up at the AMA threshold over the course of 1989-2002 appears to imply that, on net, amniocentesis and prenatal screening tests for Down syndrome are substitute goods. While—unlike an amniocentesis—a prenatal screening test provides imperfect information (in the sense that it only estimates the *likelihood* that the fetus has Down syndrome), the fact that prenatal screening tests typically only require an ultrasound or sample of the mother's blood means that screening tests present essentially zero risk to the fetus. Given that an amniocentesis is arguably costlier for older women (it more difficult for older women to "replace" an amniocentesis-caused miscarriage with another pregnancy), this reduction in risk appears to have induced a significant fraction of women at the AMA amniocentesis eligibility cutoff to forgo an amniocentesis, and to rely instead only on the information provided by prenatal screening tests for Down syndrome.

The Effect of Amniocentesis Eligibility on Down syndrome Incidence

I next explore whether there is a noticeable discontinuity in Down syndrome incidence at the amniocentesis eligibility threshold to match the significant increase in amniocentesis take-up that I observe at age 35. Since an amniocentesis is typically performed early in the second trimester of pregnancy, one important way women could act on a positive amniocentesis result is by terminating the pregnancy. As I touched upon in the "Empirical Strategy" section of this paper, if a substantial fraction of women who undergo an amniocentesis and learn that the fetus has Down syndrome choose to terminate the pregnancy, this would likely be reflected in a sizeable decrease in Down syndrome incidence at the amniocentesis eligibility threshold.

To econometrically estimate whether there is a shift in Down syndrome incidence at the amniocentesis eligibility threshold, I estimate equation (2) for the years 1989 to 2002 combined. Table 4 presents the results from these regressions. Identical in setup up to Table 2, Column 1 of Table 4 includes no additional controls, and Column 2 includes controls for a host of baseline maternal and paternal characteristics, such as the mother and father's race and ethnicity and the mother's educational attainment. Consistent with Figure 7, Columns 1 and 2 in Table 4 provide no evidence that there is a significant shift in Down syndrome incidence at the AMA amniocentesis eligibility threshold. In fact, the estimated coefficient on *AMA* in Column 2 of Table 4 suggests that, over the entire sample period, the probability of having a child with Down syndrome increased by 0.004 percentage points at the amniocentesis eligibility threshold. (This result is not statistically significant at conventional levels.)

Like Column 4 in Table 2, Column 4 in Table 4 includes an indicator variable that equals one if the year is at least 1996 (the year in which the quadruple screen was introduced), as well as interactions between this indicator variable (*Post-1996*) and *AMA*, *Age – 35*, and *(Age – 35)*AMA*. Since the results presented in Table 3 and Figure 9 provide strong evidence that women began to substitute away from an amniocentesis in the mid-1990s, if the results of an amniocentesis had a substantial impact on women's behavior or the informational value of an amniocentesis changed over this time period, one may expect to see a differential shift in the effect of amniocentesis eligibility on Down syndrome incidence in the post-1996 period. Notably, however, the estimated coefficient on *(Post-1996)*AMA* is statistically insignificant.[12]

[12] Ideally, I would also estimate equation (2) separately for each year in my sample, as I do for amniocentesis use, but the rarity of Down syndrome means that I lack the statistical power to precisely do so.

Table 4, The Effect of Amniocentesis Eligibility on Down syndrome Incidence, All Years (1989-2002 Combined)

	(1)	(2)	(3)	(4)
AMA	0.00005	0.00004	0.00004	0.00005
	(0.00002)	(0.00002)	(0.00002)	(0.00003)
Age – 35	0.00003***	0.00004***	0.00004***	-0.00003***
	(0.00000)	(0.00000)	(0.00000)	(0.00000)
(Age – 35)*AMA	0.00003	0.00003	0.00003	0.00008**
	(0.00002)	(0.00002)	(0.00002)	(0.00002)
Post-1996				-0.00033***
				(0.00006)
(Post-1996)*AMA				-0.00001
				(0.00001)
(Post-1996)*(Age – 35)				0.00012***
				(0.00000)
(Post-1996)*(Age – 35)*AMA				-0.00009***
				(0.00001)
Non-white Mother		-0.00015*	-0.00014*	-0.00014*
		(0.00006)	(0.00006)	(0.00006)
Hispanic Mother		-0.00019	-0.00018	-0.00018
		(0.00016)	(0.00016)	(0.00016)
Mother Did Not Complete High School		0.00002	0.00002	0.00002
		(0.00007)	(0.00007)	(0.00007)
Mother Completed Some College		-0.00010	-0.00010	-0.00010
		(0.00005)	(0.00005)	(0.00005)
Mother Graduated College		-0.00021**	-0.00020**	-0.00020**
		(0.00007)	(0.00007)	(0.00007)
Mother is Married		0.00002	0.00002	0.00002
		(0.00008)	(0.00008)	(0.00008)
Father's Age		-0.00001	-0.00001	-0.00001
		(0.00000)	(0.00000)	(0.00000)
Non-white Father		-0.00016	-0.00016	-0.00016
		(0.00008)	(0.00008)	(0.00008)
Hispanic Father		-0.00012	-0.00012	-0.00012
		(0.00010)	(0.00010)	(0.00010)
Constant	0.00058***	0.00103***	0.00130***	0.00125***
	(0.00000)	(0.00011)	(0.00019)	(0.00016)
Year Fixed Effects	No	No	Yes	Yes
Mean of Dependent Variable	*0.0006*	*0.0006*	*0.0006*	*0.0006*
N	*1,606,152*	*1,606,152*	*1,606,152*	*1,606,152*
R^2	*0.00001*	*0.00005*	*0.00006*	*0.00007*

The dependent variable is an indicator variable that equals one if Down syndrome was reported on the birth certificate. All regressions were estimated using a bandwidth of two (i.e., only women ages 33 to 37 (inclusive) were included in the sample). AMA is an indicator variable that equals one if the mother was at least age 35 at the birth of her child, and Post-1996 is an indicator variable that equals one if the year is at least 1996. Standard errors are clustered by mother's age, and standard errors are given in parentheses.

$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

It is important to acknowledge, however, that the lack of a statistically meaningful relationship between amniocentesis eligibility and Down syndrome incidence may be partially due to a lack of statistical power. After all, Down syndrome is a rare genetic condition, and Figure 4 suggests that there is systematic underreporting of Down syndrome in the Vital Statistics data. The rarity of Down syndrome—combined with underreporting and the fact that amniocentesis take-up is far less than 100% at the eligibility threshold—may simply mean that my empirical strategy would not be able to detect a link between amniocentesis eligibility and Down syndrome incidence, even if such a link existed.

Furthermore, Vital Statistics *birth* data is not the optimal dataset with which to explore whether there are "missing children" with Down syndrome at the amniocentesis eligibility cutoff, since Vital Statistics birth data only captures the prenatal genetic testing choices and birth outcomes of babies who were actually born. Ideally, to determine the extent to which women terminated pregnancies where an amniocentesis reveals that the fetus has Down syndrome, I would analyze data that described every *pregnancy* in the U.S. over the period from 1989 to 2002. Unfortunately, such a dataset does not (yet) exist.

In an effort to address these limitations, I implement an alternative regression specification that estimates the effect of amniocentesis eligibility on the number of first births for my sample period of 1989 to 2002. This alternative specification requires me to aggregate my dataset to the maternal age-year level, and as a result, this regression specification may be better able to capture any shifts in the overall birth distribution at age 35. (A dip or "hollowing out" in the birth distribution at age 35 would be consistent with women terminating pregnancies that test positive for Down syndrome.) To implement this alternative specification, I estimate equation (2) at the maternal age-year level, changing the dependent variable to be the number of first births.

In Figure 10, I plot the distribution of first-born babies for the period from 1989 to 2002, combined.

Collapsing my data to the maternal age-year level reduces my total number of observations to 590, and as a result of this dramatic drop in sample size, I do not implement a local linear regression with a bandwidth of two. Instead, I estimate a local linear regression with a bandwidth of five. (That is, I restrict my sample to maternal ages between 30 and 40, inclusive.) I provide my results from my estimation of this alternative regression specification in Table 5. Similar in setup to Table 4, in Column 3 of Table 5, I add year fixed effects, and in Column 4, I add an indicator variable that equals one if the year is at least 1996 (the year in which the quadruple screen was introduced), and I interact this variable (*Post-1996*) with *AMA*, *Age – 35*, and *(Age – 35)*AMA*.

Figure 10

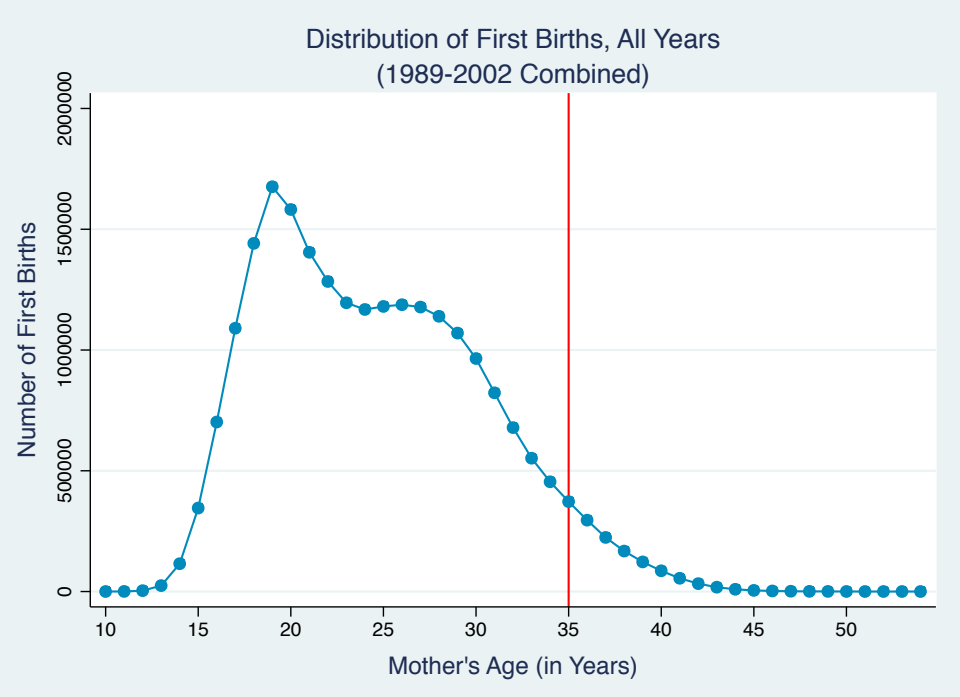


Table 5, The Effect of Amniocentesis Eligibility on the Number of First Births, All Years (1989-2002 Combined)

	(1)	(2)	(3)
AMA	3395.88**	3395.88*	3957.16*
	(1517.38)	(1587.74)	(1961.93)
Age – 35	-9221.86***	-9221.86***	-9597.79***
	(343.99)	(359.94)	(491.81)
(Age – 35)*AMA	5125.52***	5125.52***	5807.66***
	(441.36)	(461.83)	(581.66)
Post-1996			11876.50***
			(1177.70)
Post-1996*AMA			-1122.57
			(814.17)
(Post-1996)*(Age – 35)			751.86**
			(279.24)
(Post-1996)*(Age – 35)*AMA			-1364.27***
			(282.22)
Constant	21934.24***	16946.63***	15710.28***
	(1285.23)	(1414.61)	(1807.05)
Year Fixed Effects	No	Yes	Yes
Mean of Dependent Variable	*30,776*	*30,776*	*30,776*
N	*154*	*154*	*154*
R-squared	*0.9766*	*0.9945*	*0.9952*

The dependent variable is the number of first births. The regressions in all three columns were estimated using a bandwidth of five (i.e., only first-time mothers age 30 to 40 (inclusive) were included in the sample). AMA is an indicator variable that equals one if the mother was at least age 35 at the birth of her child, and Post-1996 is an indicator variable that equals one if the year is at least 1996. Data is collapsed at the maternal age-year level. Standard errors are clustered by mother's age, and standard errors are given in parentheses.
$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

The results presented in Table 5 are broadly consistent with the results presented in Table 4, and they provide no evidence that women are terminating pregnancies that test positive for Down syndrome. The point estimates on *AMA* in Columns 1 and 2 are positive, implying that the number of first births actually increased at age 35. This result is the exact opposite of what I would expect to see if a substantial fraction of women at the AMA threshold who underwent an amniocentesis and learned that the fetus had Down syndrome terminated the pregnancy. (If a substantial fraction of women at the AMA threshold terminated pregnancies that tested positive for Down syndrome, I would expect to see a "hollowing out" or "dip" in the birth distribution at

age 35; Figure 10 also provides no visual evidence of such a dip.) Furthermore, while the point estimate on (*Post-1996*)**AMA* is negative, it is statistically insignificant at conventional levels, indicating that there was not a differential shift in the number of first births to AMA women in the pre-1996 and post-1996 periods.

Lastly, returning to my primary analysis sample of all births to first-time mothers between the ages of 33 and 37, I investigate whether there is a discontinuity in any broader measures of infant health at the amniocentesis eligibility cutoff. In particular, I explore whether there is a discontinuity in the probability that the baby is born with any chromosomal abnormality, the probability that the baby is born at a low birth weight (less than 2,500 grams and greater than or equal to 1,500 grams), the probability that the baby is born at a very low birth weight (less than 1,500 grams), the baby's 5-minute Apgar score, and the probability that the baby has a five-minute Apgar score less than seven at age 35.[13] (As mentioned in the "Data" section of this paper, babies with Apgar scores of at least seven are generally considered to be in good health.)

Table 6 reports the results from this set of regressions. Using each of these five measures of infant health as the dependent variable, I estimate equation (2) within a two-year bandwidth of the amniocentesis eligibility threshold. I fail to detect improvements in *any* of these infant health outcomes at the amniocentesis eligibility threshold. The results in Table 6 actually suggest that (1) the probability the baby has any chromosomal abnormality or neural tube defect, (2) the probability the baby is born at a low birth weight, and (3) the probability that the baby's five-

[13] While amniocentesis is primarily used to detect Down syndrome, an amniocentesis will also detect other chromosomal abnormalities or neural tube defects, which are birth defects of the spine, spinal cord, and brain.

minute Apgar score is less than seven, actually *increase* at the amniocentesis eligibility cutoff. (While statistically significant, it is important to note that these coefficients are quite small relative to the mean, so the reader should be cautious in her interpretation of the economic significance of these point estimates.)

Table 6, The Effect of Amniocentesis Eligibility on Broader Indicators of Infant Health, All Years (1989-2002 Combined)

Dependent Variable	(1) *Child Has a Chromosomal Abnormality or Neural Tube Defect*	(2) *Child's 5-Minute Apgar Score*	(3) *Child's 5-Minute Apgar Score is Below 7*	(4) *Child is Born at a Low Birth Weight (<2,500 grams and ≥1,500 grams)*	(5) *Child is Born at a Very Low Birth Weight (<1,500 grams)*
AMA	0.00010*	-0.00573**	0.00113***	0.00206***	0.00007
	(0.00004)	(0.00078)	(0.00000)	(0.00022)	(0.00018)
Age – 35	0.00005***	-0.00351***	0.00011**	0.00269***	0.00092***
	(0.00001)	(0.00012)	(0.00003)	(0.00005)	(0.00001)
(Age – 35)*AMA	0.00012**	-0.00413***	0.00023***	0.00129***	0.00031
	(0.00003)	(0.00069)	(0.00000)	(0.00019)	(0.00016)
Constant	0.00162***	8.85835***	0.01999***	0.08932***	0.02103***
	(0.00032)	(0.00748)	(0.00141)	(0.00255)	(0.00056)
Controls	Yes	Yes	Yes	Yes	Yes
Mean of Dependent Variable	*0.0011*	*8.8830*	*0.0135*	*0.0739*	*0.0185*
N	*1,300,488*	*1,300,488*	*1,300,488*	*1,300,488*	*1,300,488*
R^2	*0.00006*	*0.00129*	*0.00106*	*0.00358*	*0.00308*

The regressions in all columns were estimated using a bandwidth of two (i.e., only women ages 33 to 37 (inclusive) were included in the sample). AMA is an indicator variable that equals one if the mother was at least age 35 at the birth of her child, and a child was considered to have a chromosomal abnormality and/or neural tube defect if Down syndrome, anencephaly, spina bifida/meningocele, and/or "other chromosomal abnormality" was reported on the child's birth certificate. Each regression controls for the mother and father's race and ethnicity, the mother's educational attainment, the mother's marital status, and the father's age. Standard errors are clustered by mother's age, and standard errors are given in parentheses. $^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$.

Section 7: Robustness Checks and Falsification Tests

To ensure that the results presented above were not sensitive to my choice of bandwidth, I re-estimated equations (1) and (2) for the combined period of 1989-2002 with an assortment of different bandwidths. Reassuringly, my results are qualitatively consistent with a variety of bandwidths, from three to ten, and these alternative results are given in Tables 7 and 8.[14]

As an additional robustness check, I implemented a series of falsification tests, where I estimated equation (1), but instead of placing the amniocentesis eligibility cutoff at 35, I placed the amniocentesis eligibility cutoff at each maternal age from 20 to 43. Considering that the amniocentesis eligibility cutoff is located at age 35, the $\hat{\delta}_A$'s at maternal ages other than 35 should be close to zero and statistically insignificant. A graph of the estimated coefficients from these falsification tests is given in Figure 11.

As Figure 11 clearly demonstrates, the $\hat{\delta}_A$'s from the regressions implemented with these fake amniocentesis eligibility cutoffs hovered close to zero, with the exception of the $\hat{\delta}_A$ on 36. Importantly, however, the apparent drop in amniocentesis take-up at 36 can be explained by the fact that the actual amniocentesis eligibility cutoff is located at age 35, the maternal age immediately before 36. Since there was a sharp increase in amniocentesis take-up at age 35 (see

[14] While qualitatively consistent with the results provided in Table 2, the results depicted in Table 10 show that as the bandwidth increases, the magnitude of the point estimate on *AMA* increases. This seemingly odd result is due to several factors. First, a line is an increasingly poor fit for the underlying relationship between maternal age and amniocentesis take-up as more ages are included in the sample, biasing the estimated coefficient on *AMA*. Second, while the slope of the regression line on the right-hand side of the cutoff is roughly the same across all bandwidths, the slope of the regression line on the left-hand side of the cutoff becomes noticeably shallower as the bandwidth increases. This combination of a shallower slope on the left-hand side of the cutoff—which is driven by the inclusion of more and more non-AMA women who did not undergo an amniocentesis into the sample—with a stable slope on the right hand side of the cutoff, pushes the point estimate on *AMA* upwards as the bandwidth increases.

Table 2), and equation (1) allows the slopes of the regression lines to be different on either side of the eligibility cutoff, the $\hat{\delta}_A$ on 36 is negative (and nearly equal to magnitude to the $\hat{\delta}_A$ on 35) because the *actual* change in amniocentesis take-up at 36 is far less than what the change in amniocentesis take-up at 36 *should have been* if amniocentesis take-up had continued to increase at the rate it did from age 34 to age 35. In other words, the $\hat{\delta}_A$ on 36 is consistent with what I would expect to see, assuming that the only discontinuity in amniocentesis take-up was located at age 35.

Table 7 The Effect of Amniocentesis Eligibility on Amniocentesis Take-up (All Years 1989-2002 Combined), Estimated Separately for Bandwidth=2 to Bandwidth=10

	(1) **BW=2**	(2) **BW=3**	(3) **BW=4**	(4) **BW=5**	(5) **BW=6**	(6) **BW=7**	(7) **BW=8**	(8) **BW=9**	(9) **BW=10**
AMA	0.0617***	0.0755***	0.0841***	0.0907***	0.0961***	0.1010***	0.1054***	0.1091***	0.1123***
	(0.0018)	(0.0065)	(0.0086)	(0.0091)	(0.0091)	(0.0090)	(0.0090)	(0.0090)	(0.0089)
Age – 35	0.0228***	0.0140***	0.0098***	0.0073***	0.0057***	0.0045***	0.0037***	0.0030***	0.0025***
	(0.0001)	(0.0021)	(0.0023)	(0.0020)	(0.0017)	(0.0014)	(0.0012)	(0.0010)	(0.0009)
(Age – 35)*AMA	-0.0019	0.0041	0.0069**	0.0088***	0.0096***	0.0099***	0.0101***	0.0101***	0.0101***
	(0.0015)	(0.0027)	(0.0027)	(0.0024)	(0.0021)	(0.0020)	(0.0020)	(0.0019)	(0.0019)
Non-white Mother	-0.0123**	-0.0109**	-0.0095**	-0.0085**	-0.0076***	-0.0066***	-0.0059***	-0.0052***	-0.0048***
	(0.0044)	(0.0040)	(0.0034)	(0.0029)	(0.0025)	(0.0022)	(0.0019)	(0.0017)	(0.0015)
Hispanic Mother	-0.0176**	-0.0160**	-0.0136**	-0.0119***	-0.0103***	-0.0089***	-0.0079***	-0.0069***	-0.0062***
	(0.0057)	(0.0048)	(0.0042)	(0.0036)	(0.0031)	(0.0026)	(0.0022)	(0.0019)	(0.0016)
Mother Did Not Complete High School	-0.0238*	-0.0205**	-0.0180**	-0.0156**	-0.0134**	-0.0116**	-0.0096**	-0.0078**	-0.0065***
	(0.0095)	(0.0079)	(0.0068)	(0.0059)	(0.0050)	(0.0041)	(0.0034)	(0.0028)	(0.0023)
Mother Completed Some College	0.0134**	0.0114**	0.0097**	0.0084**	0.0071**	0.0061**	0.0052**	0.0043**	0.0037**
	(0.0047)	(0.0041)	(0.0035)	(0.0030)	(0.0026)	(0.0022)	(0.0019)	(0.0016)	(0.0014)
Mother Graduated College	0.0337**	0.0285**	0.0243**	0.0207**	0.0175**	0.0150**	0.0128**	0.0110**	0.0096**
	(0.0093)	(0.0085)	(0.0076)	(0.0067)	(0.0058)	(0.0051)	(0.0045)	(0.0040)	(0.0036)
Mother is Married	-0.0057***	-0.0055***	-0.0052***	-0.0047***	-0.0044***	-0.0042***	-0.0040***	-0.0038***	-0.0036***
	(0.0009)	(0.0013)	(0.0013)	(0.0012)	(0.0011)	(0.0011)	(0.0010)	(0.0010)	(0.0010)
Father's Age	0.0011***	0.0010***	0.0009***	0.0008***	0.0007***	0.0007***	0.0006***	0.0006***	0.0005***
	(0.0002)	(0.0002)	(0.0002)	(0.0002)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)
Non-white Father	-0.0195**	-0.0168**	-0.0144**	-0.0120**	-0.0103**	-0.0090**	-0.0080***	-0.0072***	-0.0064***
	(0.0053)	(0.0048)	(0.0044)	(0.0040)	(0.0036)	(0.0031)	(0.0027)	(0.0024)	(0.0022)
Hispanic Father	-0.0178**	-0.0153**	-0.0137**	-0.0114**	-0.0098***	-0.0083***	-0.0071***	-0.0064***	-0.0057***
	(0.0053)	(0.0050)	(0.0043)	(0.0037)	(0.0031)	(0.0025)	(0.0021)	(0.0017)	(0.0015)
Constant	0.0326**	0.0275**	0.0246**	0.0229**	0.0224**	0.0218**	0.0210**	0.0203**	0.0197***
	(0.0088)	(0.0078)	(0.0086)	(0.0087)	(0.0084)	(0.0080)	(0.0076)	(0.0072)	(0.0069)
Mean of Dependent Variable	0.0258	0.0258	0.0258	0.0258	0.0258	0.0258	0.0258	0.0258	0.0258
N	*1,679,707*	*2,430,930*	*3,272,574*	*4,208,341*	*5,209,431*	*6,247,423*	*7,297,430*	*8,334,741*	*9,342,971*
R^2	*0.0462*	*0.0579*	*0.0672*	*0.0740*	*0.0784*	*0.0806*	*0.0813*	*0.0810*	*0.0804*

The dependent variable is an indicator variable that equals one if the mother underwent an amniocentesis. Column one corresponds to an estimation of equation (1) with a bandwidth of two, column two corresponds to an estimation of equation (1) with a bandwidth of three, etc. AMA is an indicator variable that equals one if the mother was at least age 35 at the birth of her child. Standard errors are clustered by mother's age, and standard errors are given in parentheses.

$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

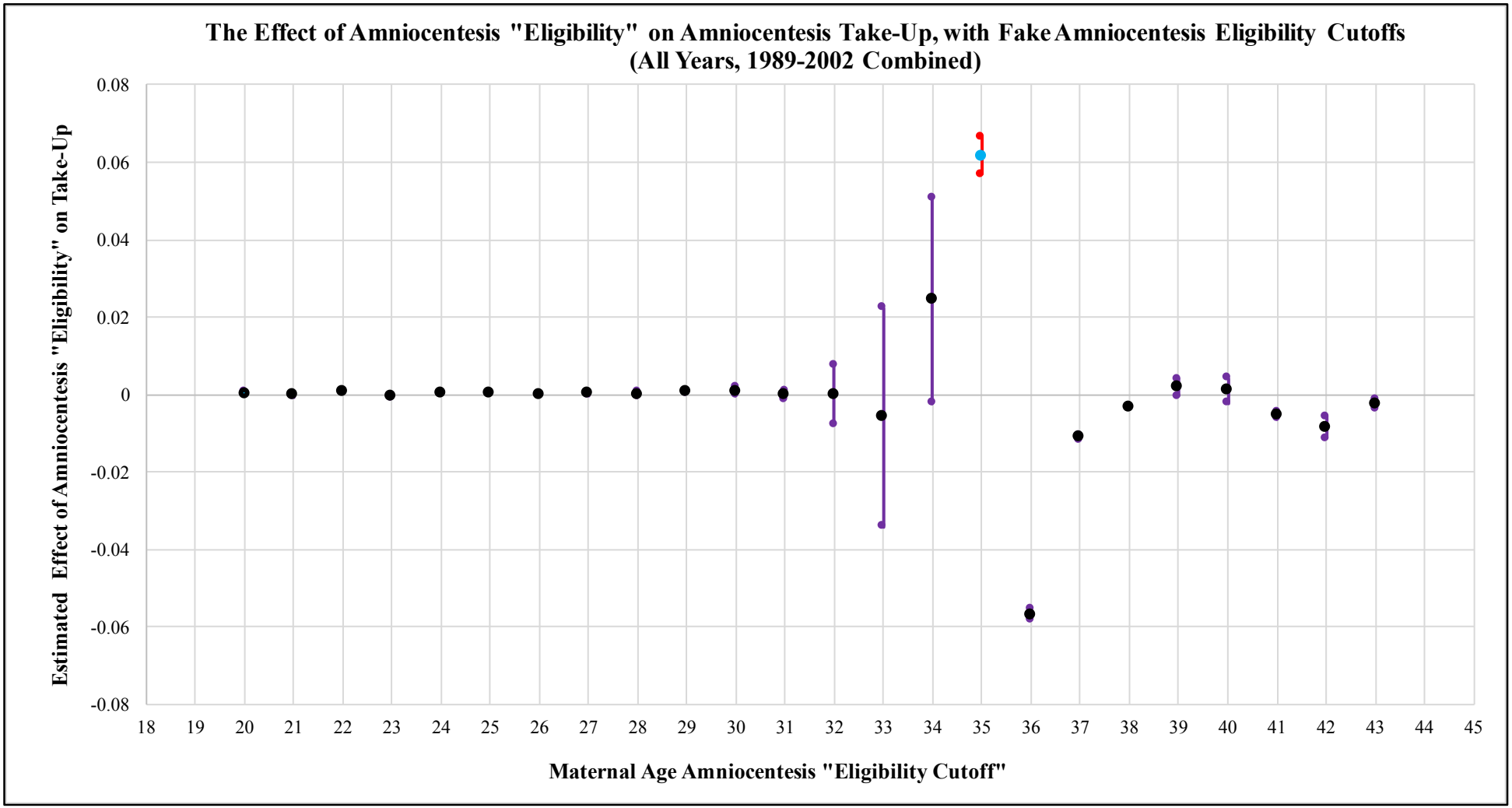
Table 8, The Effect of Amniocentesis Eligibility on Down syndrome Incidence (All Years 1989-2002 Combined), Estimated Separately for Bandwidth=2 to Bandwidth=10

	(1) **BW=2**	(2) **BW=3**	(3) **BW=4**	(4) **BW=5**	(5) **BW=6**	(6) **BW=7**	(7) **BW=8**	(8) **BW=9**	(9) **BW=**
AMA	0.00004	0.00000	-0.00008	-0.00007	-0.00005	-0.00005	-0.00003	-0.00004	-0.000
	(0.00002)	(0.00005)	(0.00008)	(0.00007)	(0.00008)	(0.00009)	(0.00009)	(0.00010)	(0.000
Age – 35	0.00004***	0.00005***	0.00007***	0.00006***	0.00005***	0.00004***	0.00004***	0.00003***	0.0000
	(0.00000)	(0.00000)	(0.00001)	(0.00001)	(0.00001)	(0.00001)	(0.00001)	(0.00001)	(0.000
(Age – 35)*AMA	0.00003	0.00007*	0.00009**	0.00011***	0.00014***	0.00016***	0.00017***	0.00019***	0.0001
	(0.00002)	(0.00003)	(0.00004)	(0.00003)	(0.00003)	(0.00002)	(0.00002)	(0.00003)	(0.000
Non-white Mother	-0.00015*	-0.00024**	-0.00026***	-0.00021***	-0.00020***	-0.00019***	-0.00018***	-0.00016***	-0.0001
	(0.00006)	(0.00007)	(0.00006)	(0.00006)	(0.00005)	(0.00004)	(0.00004)	(0.00004)	(0.000
Hispanic Mother	-0.00019	-0.00010	-0.00008	-0.00007	-0.00008	-0.00007	-0.00006	-0.00004	-0.000
	(0.00016)	(0.00013)	(0.00010)	(0.00008)	(0.00007)	(0.00006)	(0.00005)	(0.00005)	(0.000
Mother Did Not Complete High School	0.00002	0.00001	-0.00007	-0.00007	-0.00004	-0.00003	-0.00000	-0.00001	-0.000
	(0.00007)	(0.00005)	(0.00007)	(0.00005)	(0.00005)	(0.00004)	(0.00004)	(0.00004)	(0.000
Mother Completed Some College	-0.00010	-0.00010**	-0.00009**	-0.00009***	-0.00009***	-0.00008***	-0.00006**	-0.00003	-0.000
	(0.00005)	(0.00004)	(0.00003)	(0.00002)	(0.00002)	(0.00002)	(0.00002)	(0.00003)	(0.000
Mother Graduated College	-0.00021**	-0.00016**	-0.00016**	-0.00014***	-0.00014***	-0.00012***	-0.00010***	-0.00008**	-0.0000
	(0.00007)	(0.00006)	(0.00005)	(0.00004)	(0.00003)	(0.00004)	(0.00003)	(0.00003)	(0.000
Mother is Married	0.00002	0.00004	0.00005	0.00005	0.00005	0.00005*	0.00005**	0.00003	0.000
	(0.00008)	(0.00006)	(0.00005)	(0.00004)	(0.00003)	(0.00003)	(0.00002)	(0.00002)	(0.000
Father's Age	-0.00001	-0.00001	-0.00001	-0.00001*	-0.00000*	-0.00000**	-0.00000*	-0.00000**	-0.0000
	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.000
Non-white Father	-0.00016	-0.00008	-0.00005	-0.00009	-0.00008	-0.00006	-0.00006	-0.00008*	-0.000
	(0.00008)	(0.00008)	(0.00006)	(0.00006)	(0.00005)	(0.00005)	(0.00004)	(0.00004)	(0.000
Hispanic Father	-0.00012	-0.00007	-0.00001	0.00000	-0.00001	-0.00003	-0.00004	-0.00005	-0.000
	(0.00010)	(0.00007)	(0.00007)	(0.00006)	(0.00005)	(0.00004)	(0.00004)	(0.00004)	(0.000
Constant	0.00103***	0.00097***	0.00097***	0.00091***	0.00085***	0.00082***	0.00075***	0.00074***	0.0007
	(0.00011)	(0.00015)	(0.00012)	(0.00011)	(0.00011)	(0.00010)	(0.00011)	(0.00010)	(0.000
Mean of Dependent Variable	*0.00036*	*0.00036*	*0.00036*	*0.00036*	*0.00036*	*0.00036*	*0.00036*	*0.00036*	*0.000*
N	*1,606,152*	*2,325,058*	*3,130,853*	*4,027,065*	*4,986,486*	*5,981,891*	*6,989,279*	*7,985,800*	*8,955,*
R^2	*0.00005*	*0.00006*	*0.00010*	*0.00013*	*0.00015*	*0.00017*	*0.00017*	*0.00019*	*0.000*

The dependent variable is an indicator variable that equals one if the mother underwent an amniocentesis. Column one corresponds to an estimation of equation (1) with a bandwidth of two, column two corresponds to an estimation of equation (1) with a bandwidth of three, etc. AMA is an indicator variable that equals one if the mother was at least age 35 at the birth of her child. Standard errors are clustered by mother's age, and standard errors are given in parentheses.

$^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$

Figure 11



Notes: The purple bands around each point estimate are 95% confidence intervals. The point estimate given in blue is equal to the estimated coefficient on *AMA* in Column 2 of Table 2 (i.e., it is the actual estimated effect of amniocentesis eligibility on amniocentesis take-up).

Section 8: Conclusion

My investigation of the effect of women's access to prenatal genetic testing for Down syndrome on test utilization and corresponding birth outcomes reveals three key results. First, I find that becoming eligible for an amniocentesis—the most common diagnostic test for Down syndrome—had a significant impact on women's prenatal genetic testing decisions. Over the period from 1989 to 2002, I find that the probability that a woman underwent an amniocentesis increased by 6.17 percentage points at age 35, the location of the amniocentesis eligibility threshold. While this increase may seem small when viewed out of context, this 6.17 percentage point increase translates to a 62% increase over the mean amniocentesis take-up rate in my preferred sample (which consists only of first-time mothers age 33 to 37), and to a staggering 239% increase over the mean amniocentesis take-up rate for my full sample of first-time mothers.

Second, I find that the increase in amniocentesis take-up at age 35 decreased substantially over the course of 1989 to 2002. Given that the 1990s were marked by the introduction of prenatal screening tests for Down syndrome—which, unlike an amniocentesis, presented essentially zero risk to the fetus—this clear downward trend in amniocentesis take-up at age 35 implies that many women at the amniocentesis eligibility threshold were substituting away from amniocentesis, and choosing instead to rely only on the results of prenatal screening tests for Down syndrome. Even though these prenatal screenings tests are less accurate than an amniocentesis—prenatal screening tests can only estimate the likelihood that the fetus has Down syndrome—the strong downward time trend in amniocentesis take-up at age 35 suggests that

many women at the amniocentesis eligibility threshold were willing to accept this increased uncertainty in order to minimize the risk presented to the fetus.

Third, despite the clear increase in amniocentesis take-up at age 35, I find no evidence that women *acted* on the results provided by an amniocentesis. I find no evidence of a decrease in Down syndrome incidence at the amniocentesis eligibility threshold (which would be consistent with women terminating pregnancies in which the fetus tested positive for Down syndrome), and I also find no improvements along other broader measures of infant health, such as birth weight and the infant's five-minute Apgar score.[15]

It is possible, however, that AMA women benefited from an amniocentesis in ways that are unobservable in the Vital Statistics data. That is, rather than using the results of an amniocentesis to decide whether to terminate the pregnancy, parents may have utilized the results of an amniocentesis to better prepare for the type of care their child would need during and after birth. For example, parents who learned that their child has Down syndrome may have enrolled in support groups, restructured their health insurance plans to accommodate the types of health care services their child would eventually need, or moved closer to relatives or friends who would be able to help provide care.

While these are certainly important ways in which AMA women could have benefited from an amniocentesis, the fact that I find no evidence that women terminated pregnancies that tested positive for Down syndrome—combined with the fact that amniocentesis take-up was far less than 100% at the AMA threshold—leads me to question whether 35 was, in fact, the optimal location for the amniocentesis eligibility cutoff. In 1978, when no prenatal screening tests for Down syndrome were available, the NIH's placement of the amniocentesis eligibility cutoff at

[15] It is important to acknowledge, however, that these results may be partially driven by low statistical power.

age 35 seemed logical: While imperfect, maternal age is a reasonable proxy for the likelihood that the fetus will have Down syndrome, and Down syndrome risk does begin to increase substantially once a woman reaches about 30 years old (see Figure 4).

By placing the amniocentesis eligibility cutoff at age 35, however, the NIH may have unwittingly restricted amniocentesis access to women who were the *least incentivized* to both undergo and act upon an amniocentesis. Raising a child with Down syndrome carries heavy pecuniary and non-pecuniary costs: Health care costs for children with Down syndrome are roughly 12 times higher than those of a typical child, and children with Down syndrome generally require around-the-clock care, which can take a large emotional toll on the child's entire family (Boulet, et al., 2008). AMA women—and in particular, AMA women expecting their first child—may simply be more willing to shoulder these costs, since it is uncertain when—or even if—they could "replace" an amniocentesis-caused miscarriage or intentionally-terminated pregnancy. My results, which (1) show a fairly small effect of amniocentesis eligibility on take-up in absolute terms, and (2) provide no evidence that AMA women terminated pregnancies that tested positive for Down syndrome, are broadly consistent with this story.

Younger (non-AMA) women may be less willing—or even unable—to absorb these costs, and thus may have a differentially greater incentive to undergo an amniocentesis *and* terminate pregnancies that test positive for Down syndrome. In this case, then, the informational value of an amniocentesis is likely higher for younger, non-AMA women. If the NIH's goal was to place the amniocentesis eligibility cutoff at an age where the value of the informational content from an amniocentesis was highest, perhaps the cutoff should have been located at a

younger age, particularly when amniocentesis was the only available prenatal genetic test for Down syndrome.

Of course, the argument for placing the amniocentesis eligibility cutoff at a younger age is grounded in the assumption that women are rational actors, or that women would choose to undergo an amniocentesis only if the benefits exceeded the costs. If this is not the case, and instead, women blindly follow their doctor's prenatal genetic testing recommendations, then lowering the amniocentesis eligibility cutoff would potentially have had significant negative ramifications. In this scenario, thousands of additional women would likely have undergone an uncomfortable and expensive procedure that provided them little to no benefit.

In the coming years and decades, genetic tests will likely become an increasingly important part of our lives. It is unclear, however, to what extent my results can be extrapolated to other settings. In other contexts, individuals may not have the option between screening and diagnostic tests, and the benefits of undergoing a genetic test may differ depending on whether the test reveals information about a fetus (like prenatal genetic testing for Down syndrome) or about the individual herself (like genetic testing for Huntingdon's disease). Moreover, Down syndrome is an "untreatable" genetic condition, meaning that a woman's incentives to undergo prenatal genetic testing for Down syndrome may be quite different, for example, than her incentives to undergo a genetic test that can detect mutations in the two known breast cancer genes (BRCA 1 and BRCA 2). Unlike prenatal genetic testing for Down syndrome, if a woman receives a positive result on her BRCA gene test, she can actually take preventative measures to minimize her risk of developing breast cancer. As scientists continue to develop a better understanding of the human genome, individuals will likely face a host of difficult genetic

testing decisions like those outlined above, and these decisions—which can have large consequences for the healthcare system—deserve the attention of future research.

Appendix Table 1, The Effect of Amniocentesis Eligibility on Baseline Characteristics, All Years (1989-2002 Combined)

Dependent Variable:	*(1) Mother is Non-White*	*(2) Mother is Hispanic*	*(3) Mother is Married*	*(4) Mother Did Not Complete High School*	*(5) Mother Completed High School*	*(6) Mother Completed Some College*
AMA	-0.00574***	0.00038	-0.00007	0.00006	-0.00156**	0.00148*
	(0.00026)	(0.00025)	(0.00005)	(0.00019)	(0.00033)	(0.00051)
Age-35	0.00197***	-0.00137***	-0.00340***	-0.00021***	0.00042***	-0.00031***
	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)
(Age-35)*AMA	-0.00083*	0.00116**	-0.00228***	0.00100**	-0.00176**	-0.00046
	(0.00023)	(0.00022)	(0.00005)	(0.00017)	(0.00028)	(0.00044)
Constant	0.15439***	0.07854***	0.91932***	0.03083***	0.19322***	0.22038***
	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)
Mean of Dependent Variable	*0.1626*	*0.0860*	*0.8672*	*0.0387*	*0.2029*	*0.2219*
N	*1,635,188*	*1,635,188*	*1,635,188*	*1,635,188*	*1,635,188*	*1,635,188*
R^2	*0.00001*	*0.00002*	*0.00049*	*0.00001*	*0.00001*	*0.00000*

Dependent Variable:	*(7) Mother Completed College*	*(8) Mother Began Prenatal Care in the First Trimester*	*(9) Mother Began Prenatal Care in the Second Trimester*	*(10) Mother Began Prenatal Care in the Third Trimester*	*(11) Mother Underwent an Ultrasound*	*(12) Father is Non-White*
AMA	0.00002	-0.00112**	0.00048	0.00053***	0.00397***	-0.00567***
	(0.001)	(0.00017)	(0.00020)	(0.00005)	(0.00019)	(0.00015)
Age-35	0.00010***	-0.00031***	0.00037***	-0.00013***	0.00158***	0.00166***
	(0.000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)
(Age-35)*AMA	0.00122	-0.00011	-0.00007	0.00002	-0.00165***	-0.00102**
	(0.001)	(0.00015)	(0.00018)	(0.00004)	(0.00016)	(0.00013)
Constant	0.55557***	0.93765***	0.05073***	0.00844***	0.64893***	0.14592***
	(0.000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)	(0.00000)
Mean of Dependent Variable	*0.5365*	*0.9280*	*0.0585*	*0.0111*	*0.6443*	*0.1437*
N	*1,635,188*	*1,635,188*	*1,635,188*	*1,635,188*	*1,635,188*	*1,635,188*
R^2	*0.00000*	*0.00002*	*0.00001*	*0.00000*	*0.00005*	*0.00002*

Appendix Table 1, Continued

Dependent Variable:	*(13)* *Father is Hispanic*
AMA	0.00205**
	(0.00028)
Age-35	-0.00230***
	(0.00000)
(Age-35)*AMA	0.00202**
	(0.00024)
Constant	0.07000***
	(0.00000)
Mean of Dependent Variable	*0.0751*
N	*1,635,188*
R^2	*0.00002*

The dependent variable is given in the column title. The regressions in both columns were estimated using a bandwidth of two (i.e., only women ages 33 to 37 (inclusive) were included in the sample). AMA is an indicator variable that equals one if the mother was at least age 35 at the birth of her child. Standard errors are clustered by mother's age, and standard errors are given in parentheses. $^{*}p < 0.10$, $^{**}p < 0.05$, $^{***}p < 0.01$.

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